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Cd.

C O N T E N T S.

P r e f a c e.

Pages.

CHAPTER I.

Introduction 1 - 8

CHAPTER II.

Etiology 9 - 17

CHAPTER III.

Symptomatology 18 - 41

CHAPTER IV.

Blood 42 - 56

CHAPTER V.

Urine and Faeces 57 - 65

CHAPTER VI.

Age of Onset - Duration; Sex 66 - 68

CHAPTER VII.

Morbid Anatomy - Pathology 69 - 154

CHAPTER VIII.

Diagnosis 155 - 161

CHAPTER IX.

Prognosis 162 - 163

CHAPTER X.

Treatment 164 - 167

CONTENTS. (Cont^d)

Pages.

CHAPTER XI.

Conclusions	168 - 171
CLINICAL CASES.	172 - 262
Table I.	201
" II.	225
" III.	237
" IV.	262
Bibliography	264.

ILLUSTRATIONS. -

<u>Plates.</u>		<u>Page.</u>
Plate	I.	26
"	II.	41
"	III.	72
"	IV.	74
"	V.	76
"	VI.	79
"	VII.	81
"	VIII.	83
"	IX.	87
"	X.	99.

P R E F A C E.

The Disease called 'SPLENIC ANAEMIA' being one which has received comparatively little attention in this country, I have ventured to make it the subject of this Thesis. As far as possible, I have endeavored to base the following description, both clinical and pathological, on cases which I have had under observation during the last four years. A study of these has also enabled me to criticise the accounts given by others in some respects, for as these cases are not common, a certain amount of error has crept into what clinical records there are. The name Splenic Anaemia is a very unsatisfactory one, but any of the others which are used are even more so, and rather than suggest another which perhaps future research might show to be equally illogical, I have employed it.

The following account embraces the Etiology, Symptomatology and Morbid Anatomy of Splenic Anaemia, together with a review of what literature there is. To this I have added a suggestion as to its pathogenesis drawn from a study of my own cases. At the end, will be found the clinical records of these cases, and abstracts of those observed by others.

DOUGLAS STANLEY.

April 20th, 1894.

CHAPTER I.

LITERARY INTRODUCTION.

Now and then, in medical literature, mention is made of cases of anomalous Enlargement of the Spleen, accompanied by various general symptoms, but beyond, in most instances a short reference, little is said as to their clinical course, nosological position or pathological condition. That these references are few there is no doubt, but this may, in part be due to the fact, that in many cases no diagnosis has been made, or that the conditions present have been confounded with other diseases. The cases which form the subject of this paper are those sometimes referred to by various writers under the name of "Splenic Anaemia". This term seems to have been introduced by Griesinger, for cases of enlargement of the spleen without any accompanying increase in the number of leucocytes in the blood, but which this writer considers were a form of leucocythaemia, Bartholow (1) (p.229). As far back as 1856 Woillez (2) and in 1867 Müller (3) recorded instances of "Hypertrophy of the Spleen" and "Anaemia et Kackexia Splenica", with these characters. In more recent years others have been described either by this or similar names, but in the majority of cases, the /

the description is vague or incomplete in several points. The chief textbooks of medicine, either English or foreign, make no mention of these cases, or merely refer to them by name, or it may be, place them under the head of anomalous forms of leucocythaemia or lymphadenoma, or as indicating an uncertain manifestation of malaria or syphilis. Under the head of 'Leucocythaemia' in Reynold's System (4) (p.276) Gowers says, in speaking of the spleen and the increase of the lymphoid corpuscles it contains:- "Is not the pathological condition accounted for by the mere retention in the splenic pulp of large numbers of white corpuscles. That such retention and accumulation does actually occur can hardly be doubted. It must be the chief process in anaemia splenica, in which there is a simple hypertrophy of the spleen, similar to that which occurs in leucocythaemia, a great deficiency of red corpuscles in the blood but no excess of white". In Fagge (5) we find; - "there may be great enlargement of the spleen with anaemia, but without leukaemia. It is certainly rare."

Bristowe (6) says that cases are met with in which the spleen may undergo enlargement like that occurring in true leucocythaemia, in which the symptoms and course of /

of the disease resemble in almost all important respects those of leucocythaemia, but in which the anaemia is unattended with excess of leucocytes. (p.604.) Again, under the head of Hypertrophy of the Spleen, (p.593) the same author, after mentioning its frequent association with malaria, liver conditions and rickets, goes on to say: - "But some of the most remarkable examples of this affection (hypertrophy) are furnished by persons who have never suffered from any of the above disorders, and in whom there is no history pointing to the operation of any specific cause." Wilks and Moxon (7) (p.495) in speaking of the same condition, i.e., splenic hypertrophy and its more common causes, say: - "there are other cases in which the spleen is enlarged to a great size, and this enlargement is the chief, if not the only disease that can be discovered. Thus Mr Spencer Wells, removed a spleen weighing 6 lbs, this being the only disease discoverable in the body, and the blood not being leukaemic; and Mr Squire met with a spleen weighing 13 lbs., while the blood did not show a positive excess of white corpuscles. We have met with similar cases of simple hypertrophy of the spleen without leukaemia, both in the living and in dead subjects. They are generally, but not always, at least /

least during life, associated with anaemia,
 Those cases are the only ones that can be properly considered as pure examples of hypertrophy of the spleen; the cause of the enlargement is unknown and the accompanying clinical phenomena need further investigation. We are not now speaking of Hodgkin's disease or anaemia lymphatica, for in the cases at present under consideration the spleen tissue is normal throughout."

There is no mention of these cases in the textbook of medicine by Osler (8). The various works on diseases of children contain references to 'splenic anaemia'. Thus, West (9) (p.735) refers to the cases of enlarged spleen accompanied by anaemia as occurring in children. Ashby and Wright (10) (p.309) give a brief description of the condition, saying that: - "in anaemic children of all ages, the spleen is often enlarged and hard; to such cases the term 'splenic anaemia' is sometimes applied." These authors, however, do not seem to take up any definite position as to the nature of the disease; they go on to say, in reference to its etiology that: - "syphilis and malarial poisoning should be thought of".

Eustace Smith in his work (11) (p.237) et seq., describes /

describes what he calls 'simple hyperplasia' of the spleen in children, and after referring to rickets and syphilis as a frequent cause, adds: - "but this is not always the case, and sometimes no sign of diathetic disease or constitutional weakness is anywhere to be detected." We see, therefore, that with all these authors, there is a tendency to look upon the condition as an irregular and obscure effect of more common causes and where such cannot be advanced, the disease is somewhat summarily dismissed. Nor is any attempt made to differentiate between cases of anaemia with enlarged spleens as found in children, in association with various underlying conditions and other cases where there are none such. Three cases of 'splenic anaemia' are fairly fully described by Banti (12), in which he gives the principal clinical characters with a report of the post mortem appearances in two. This paper, has, to a large extent, formed a basis for subsequent writers, as reference is largely made to it in the records of other cases. Unfortunately Banti's account appears to be defective in many points, and this fact has given rise to misconceptions in many other instances. These will, however, be shown in the course of the present paper.

In /

In periodical literature, especially that of the last few years, we find more frequent accounts of the condition, and its right to a distinct place as a definite clinical entity is more prominently put forward. Thus, Brühl under the title of 'splénomégalie primitive' describes one case (13) very fully. He restricts this name to cases of splenic enlargement, where it is possible to exclude all the usual causes of enlargement of the spleen, as malaria, syphilis, tubercle, leucocythaemia, etc.

In 1892, Dr Walter Carr⁽¹⁴⁾, published a paper on 'Enlargement of the Spleen in Young Children', in which he gives many of the characters; but here again we find a tendency to class together cases which are probably quite distinct. Perhaps the first appearance of the disease in systematic works, at any rate in English, is an article on 'Splenic Anaemia' by Dr Crozer Griffith⁽²⁴⁾ which is very clear and succinct, but this writer does not by any means confine it to children, and that it may occur in adults there can now be little doubt. In a recent work on the blood by Labadie Lagrave⁽¹⁵⁾, there is also a chapter devoted to the disease, the title being 'Anémie Splénique Primitive'. The author, however, does /

does not seem to write from personal observation and his description is practically based on the accounts of cases given by Brühl and Banti. Consequently we find the same ideas transmitted, much as they occur in the latter writer's paper. These will be criticised in due course.

In conjunction with Dr Claude Wilson, I myself (16) described six cases in a paper read before the Clinical Society, in April 1893, and in the following month Dr. R.T. Williamson (17) recorded two "Cases of anaemia, with great enlargement of the spleen (splenic anaemia)," and which I have his permission to use. In the notes of cases given later, other instances with their references will be given.

Within the last few months I have had opportunities of observing other cases which are here recorded for the first time.

The principal thing that strikes the reader of the articles to which reference has been made is, that little attempt is made to give any nosological position to these cases, notwithstanding the fairly definite clinical picture which many of them present. What this position may be, is considered later.

It will also be perceived that the condition is not /

not common, to say the least, but probably here, as in so many other instances, a better knowledge will lead to more cases being recognised, and therefore, more fully described, instead of their being passed over as aberrant forms of other diseases. Although the number of cases I have collected both from literature and observation, may be comparatively few, they will, I think, serve as a basis on which a clinical description and pathological account may be founded, both of which, however, must be regarded as provisional in many points until more extensive observations shall have been made from future cases.

CHAPTER II.

Etiology.

The causation of splenic anaemia is extremely obscure, and, in the majority of recorded cases there is little light thrown upon it. Keeping in view the fact that the most prominent characteristic is probably the splenic enlargement, it was natural that malaria should always have been one of the first things suggested. But reviewing the history of the various cases, there has been little in any of them to support the idea. An apparent exception is the Case (No.XXV) recorded by Lodi, of a man who, at the age of 13, had tertian ague for 3 months, which however, completely disappeared ten years before any symptoms of splenic anaemia came on. Granting that the condition was true malaria, it naturally brings to one's mind the observations of Gowers on the possible influence of malaria in the causation of leucocythaemia. In all the other cases quoted, this factor has been carefully considered and all the evidence goes to show that it could be safely eliminated. This is especially so in the Cases I have already recorded, and Cases VII to XII. On the other hand Henoch (18) (vol.II, p.128) quotes a case of a mother who suffered from malaria, who had a child the /

the subject of splenic anaemia. Moreover, those cases of enlarged spleen due to malaria run a very different course, and have a very different morbid anatomy from the cases which are now described. The effect of treatment, too, is very different, and goes far to show that there is extremely little, or no, relationship between them. Thus, several of the cases referred to by Dr Wilson and myself (16) were treated with quinine, but with no effect; it has also been tried in the cases I record independently.

The question of rickets is a much more difficult one. We frequently find enlargement of the spleen accompanied by a marked anaemia in rachitic children, though Barlowe and Bury (24) (vol.II, 231) hold a contrary opinion, stating also, that even when present the anaemic and splenic enlargement are different, and belong to a separate cachexia. I hope to show later, that, in the anaemia splenic condition, and the general course of the disease, splenic anaemia really differs in all respects from the rachitic cases; and also that there seems to be a well-defined line drawn between cases of splenic anaemia so called in rachitic and children, the more profound and progressive form occurring /

occurring in adults. Dr Walter Carr (14) in his paper on 'Splenic Enlargement in Children', drawn from a series of thirty cases, admits that in only a very few is he able to eliminate rickets as a factor. Crozer Griffith states (24) that splenic anaemia may occur in children at any age as well as in adults. This is doubtless true but when occurring in early life, it is probably independent of any rachitic tendency. Thus, in the cases already referred to, there has been no sign of any rachitic element, though it was at first thought there might be, but more careful examination goes to show that this is not so. In the case of Mrs N. (No.I), there was a perfectly healthy childhood which was passed in the country. In the case of J.K., (No.II), there is nothing suggestive of rickets, notwithstanding that he has lived in Birmingham; he is an only child, and his surroundings were always healthy till recently. Prognosis, too, helps to show that there is no relationship between cases with a rachitic history and true instances of splenic anaemia, for in the former, recoveries seem to be the rule or at any rate very frequent; in the latter, as will be shown later, the chances of recovery are small.

It /

It is possible that a rachitic tendency in some few cases may have the effect of reducing the power of the blood-formative system, and thus act indirectly as a cause of future splenic anaemia. When we consider the extreme prevalence of rickets compared with the rarity of undoubted cases of the former, together with the great difference in their respective courses, we must, I think, come to the conclusion, that we are dealing with two quite different clinical and pathological conditions.

Dr T. Barlow (private communication) states it as his opinion, that the cases of enlarged spleen, in rachitic children frequently recover, and that there is a marked contrast between such patients, and splenic anaemia. We are therefore probably justified in excluding rickets as a cause of the disease to any extent.

Syphilis, being a well-known cause of enlargement of the spleen, requires consideration. Its influence in the cases of children, such as those noticed by Carr (14) is apparently more marked than in adults, and in the cases which form the subject of that author's communication there was reason to suspect its presence /

presence in several. In none of the cases of splenic anaemia given in the present paper, has it been possible to get any history pointing to syphilis, and in a large number, most certainly in all those taken from personal observation, it certainly was not present. We may probably apply the same line of argument to syphilis as was done in the case of rickets as a casual factor in those cases occurring in unhealthy children as compared with true cases of splenic anaemia; that is to say, while splenic enlargement does certainly occur in syphilitic children, this does not constitute splenic anaemia, there being considerable clinical and pathological differences between the two diseases. It does not appear justifiable to speak of syphilis as the cause of splenic anaemia, because, enlargement of the spleen and anaemia occur in children with a specific history, for, as will be shown, these points do not, in themselves, constitute splenic anaemia. The fact that cases, with a course similar to that which will be described, occur in adults as well as in children, and where there is no syphilitic history, is of more weight against splenic anaemia being due to this cause, than is the occurrence of anaemia with enlarged spleen in children the subject of syphilis, but where /

where the clinical course differs in many important points.

Other conditions, such as tubercle and alcohol, hardly require discussion. Fatigue, privation, repeated pregnancy, injury, have all been advanced as factors, but reviewing the circumstances of the various patients, we must admit that these are inadequate. Thus, the social conditions of many of the cases reported have been very good, and in those referred to in a previous paper (16) the surroundings have been of the best. No doubt, starvation, etc., may have some influence, be it predisposing or aggravating, and though in three cases, I have reported or heard of, pregnancy was present, it was obviously only a complication.

In the series of cases forming the subject of the communications to the Clinical Society, a distinct feature was the hereditary element, and, so far as I have been able to find, no other reference has been made to this as an etiological factor. In these cases it is too marked to be overlooked. Thus, the series referred to consisted of three generations, and included three distinct families. In the genealogical table (Table /

(Table No.II p.225), annexed, it is seen that the first case was a lady born in 1825, whose two eldest children were subjects of the same condition, and that the eldest had two children likewise affected, the second, a daughter distinctly affected, as well as a younger child, who seems now to be developing anaemic symptoms. The connection between these six cases seems too obvious not to be of very great importance, as an etiological element. I have also obtained a like hereditary history in connection with Cases IV, XV and XVI. The first, (No.IV), was a woman whose father, and his sister had greatly enlarged spleens, together with other symptoms, which it will be shown, are characteristic. The patient's child also had an enlarged spleen, but, as it died at an early age, the presence of accompanying conditions was uncertain. This is more fully considered in the account of the Case (q.v.)

Cases XV and XVI are those of a brother and sister that were under the care of Dr Saundby of Birmingham, who described their condition (19). Both patients had markedly enlarged spleens and other prominent symptoms, and their father was also the subject of a similar condition.

In /

In view of this distinctly hereditary condition, we must acknowledge that here we have a very definite etiological factor. As to how this may act, we shall consider later. In these three series, we find, the tendency transmitted from father to daughter in three cases (Nos. IV, VIII and XVI); from mother to son in four (Nos. IV, VII, IX, X); from father to son in one (No. XV); and from mother to daughter in one, (No. XII); showing apparently that the tendency is, for transmission to the opposite sex; and here a curious point comes in, for in Case VII, where the transmitter was a male (vide Table II, p. 225), the first child was a male and remained unaffected, while in Case XII where the transmitter was a female the first child was a female, and also remained unaffected.

Hereditary influence is not unknown in other diseases of the haemic system, as it has been noticed in leucocythaemia by Casati (20), Biermer (21), Senator (22) and others. This point is of some value as indicating that some constitutional defect in either the blood formative or destructive systems may be the underlying causes in diseases such as these.

It would seem improbable that climate has any influence on the etiology of the disease.

Reviewing, therefore, the etiology of splenic anaemia /

anaemia, we find that, with the exception of three remarkable series of cases in which heredity was a prominent feature, its origin is extremely vague, quite as much so as in leucocythaemia, lymphadenoma and other "blood diseases"; that it may appear irrespective of age or station in life.

CHAPTER III.

SYMPTOMATOLOGY.

It will be convenient, to divide the course run by 'Splenic Anaemia' into stages, notwithstanding that in some cases there may be little or no differences serving to point out the periods from each other.

The First Stage ends when the various symptoms become constant, and is very indefinite, for the invasion is extremely insidious in most instances. So much is this the case, that it is probably impossible to say when the disease began, for, as the early symptoms are so very vague, there is little on which to found a diagnosis. It is not unlikely, therefore, that the disease may be present for some years without sufficient departure from health to bring the patient under medical observation. No doubt, it is from not bearing this early and slightly marked period in mind that some writers have advanced fallacious views as to the nature of the complaint. It would seem probable from the histories of the various cases that there are considerable variations in the manner of invasion. In one group, the first thing discovered is an /

an enlarged spleen, other symptoms being almost wholly absent, so far as the patients are aware. As will be seen later (p.110) this fact has been taken largely into account by Banti in the theory he forms of the relation of the spleen to the general condition. More probably, however, in all cases in which the splenic tumour is the most obvious thing to attract notice, there have been slight manifestations of anaemia, etc. It is, however, difficult to be certain in these instances.

In the larger number of cases, there seem to be marked signs and symptoms of anaemia. In these, we find a gradual loss of energy, a more or less marked pallor of the skin/ and visible mucous membranes, and with, it may be, fainting fits, occasionally attacks of epistaxis. In some instances, this symptom was the first thing noticed; other haemorrhages may occur; such as haemoptysis, and haematemesis, but it is unusual to find any except the first at such an early period of the disease. The manifestations of anaemia at this stage may be merely temporary as shown by Case VIII, where the patient's general appearance is one of health, and only on close enquiry is it found, that at times she is pale and languid. It is only then /

then, that careful inspection of the mucous membranes and nails shows an abnormally pale condition. In the case of her younger sister[§] there is still less manifestation: all that one can say, is that she is subject to fits of langour unnatural at her age. Still I believe her to be in the earliest stage, and that probably in a couple of years, she may show definite signs, including enlargement of the spleen. In a large proportion of cases in this stage, there may not be any particular loss of appetite nor other digestive trouble, but in some there is a gradual failure and there may be attacks of vomiting, nausea and diarrhoea; this last may alternate with constipation.

With such vague symptoms, it is not surprising that the true nature of the cases may be easily overlooked, and a diagnosis of simple anaemia or dyspepsia be given, as was done in several of the cases I have collected.

In the other group, we find the first thing of which the patient complained is a feeling of weight or dragging in the left hypochondriac region, sometimes accompanied by severe stabbing pain which may radiate /

[§]This case has not been included in the series.

radiate through to the left scapula. These crises may be accompanied by pyrexia, nausea, vomiting, diarrhoea, and a considerable increase in the size of the spleen, which may also become very tender on palpation. Were the history of the point of origin of these sharp pains not very definite, they might easily be mistaken for attacks of biliary colic, the more so as even at this early stage there may be a yellow tinge of the skin. Pain is not invariable, however, nor are vomiting and diarrhoea always noticed, for in some instances I have known the patient to have a temperature up to 104° F. with great enlargement of the spleen, and practically no discomfort whatever, the whole subsiding in a week or so. In other cases, there may be splenic enlargement alone, this being perhaps discovered by accident, as in a case of my own, where the patient "felt a lump in her side" shortly after the birth of a child.

This first stage therefore, begins very vaguely and may last from a few months to two or more years, and is characterised by extremely indefinite symptoms which are often completely absent for variable periods, even for years, as in cases personally observed; the /

the earlier the stage probably the longer the periods of quiescence.

There is no sharply drawn line between the First and Second stages, but in whatever manner the earlier symptoms have supervened, there comes a time when they all show increase in their severity, and it becomes evident that the patient is suffering from some serious constitutional disease. Although intermission, even of the most severe symptoms, may still be a salient feature, the periods of quiescence are not so marked nor last so long as in the first stage. Thus, while attacks of nausea, diarrhoea, etc., may be occasionally observed, and not infrequently altogether absent in the first stage, in the second they form usually a marked symptom, although there is great variation in the way different patients are affected. They may last very much longer and resist treatment to a far greater extent than in the earlier period. Epistaxis may be frequent and severe, while other haemorrhages, very exceptional in the first stage, are not at all uncommon in this. Thus, there has been severe haematemesis, haemoptysis, passage of blood per rectum, and in some instances, considerable purpura (vide Plate p. 41)

The /

The patients may lose weight considerably, though Banti (12) lays stress on the fact that the subcutaneous fat may show no decrease. Great weakness is a marked feature, and may be more or less constant. Thus, while in the first stage, loss of strength accompanied the other symptoms when these were present, disappearing with them; it becomes more continuous, and, to a large extent, independent of the exacerbations in the second stage, the patient remaining very weak for sometime after they have passed off.

We may now describe in more detail these attacks, so characteristic of the early part of the second stage. The patient feels ill, with perhaps aching in the limbs and back, and becomes extremely weak. There may be an attack of epistaxis or other haemorrhage, and not infrequently slight rigors; the temperature is more or less elevated; vomiting and diarrhoea may be severe. The general tint of the skin, which in this stage is always more or less pallid, may become tinged with yellow amounting even to an 'attack of jaundice'. The abdomen increases in size, and there is frequently severe pain in the splenic region. There may be intense dyspnoea and palpitation on making any effort /

effort, and fainting fits of an alarming character, may also occur. The patient may also complain of buzzing in the ears and various other phenomena of cerebral anaemia. The urine is peculiarly dark-coloured during such an attack; its characters are given later under a special head. The blood shows marked decrease in the number of red corpuscles, the white remaining unaltered; the haemoglobin is also more or less reduced: vide p. 42 .

The 'jaundice' is a marked feature in the larger number of cases, and was especially so in those recorded by Dr Wilson and myself; it varies in its severity, and may apparently be more marked at an earlier period of this stage, as in one case (No. IV), where the patient formerly had it much more marked than latterly, notwithstanding that the disease is making progress. We see therefore, that in the early part of the second stage, the general severity of the symptoms has increased, and the attacks become more frequent; also their effect on the patient lasts longer.

In the case of women, there is, as a rule, total amenorrhoea.

From this condition there is a gradual increase of all the symptoms till the patient reaches what we /

we may term the fully developed second stage. It is now that the physical conditions are most marked, and may be studied more in detail.

External Appearance.

The patient now presents a more or less marked facies; thus, as in the first period the general aspect may show little alteration, and in the earlier part of this stage the patient only showed anaemia at the time of, or after, one of the attacks just described; there is now a pronounced, almost characteristic appearance. There is general pallor, with even a lemon tint, about the face, hands, feet, etc. This latter does not reach the same degree as in pernicious anaemia, but it is still sufficiently marked to be a valuable clinical feature. Added to this, there is frequently an olive tint. Thus, the cheeks, lips and conjunctival mucous membranes may be very pale, the dorsal surface of the hands and the feet may show the yellow white, or pale lemon tint, and round the brows, over the forehead and sides of the neck, the skin may be of a yellow olive colour. There is, of course, much variation in these characters, but speaking generally, the patients are liable to show appearances similar to these. /

PLATE I.

Arm showing deposit of pigment in small patches and lemon grey tint of the skin.

Vide Case III.

PLATE II.

Leg from the same case showing purpuric eruption.





these. In one case (No.III) which I have been able to keep under observation for several weeks, the lemon tint was very well marked. In some cases the skin has been described as a dusky yellow. An important point is, that in hereditary cases, as different members of a family become affected, they develop a striking similarity of complexion.

This may perhaps be the best place to describe a symptom which, although it may have nothing to do with the stage we are considering, is of very great interest; that is pigmentation, of the skin. This has been noticed in several of the cases recorded here. The pigmentation in two (Nos III & IV) was deposited in small patches over the arms, sides of the neck, etc (vide Plate I, p.26) while in two others, it was more diffuse, occupying the forehead near the roots of the hair, the axillary borders, the sides of the neck etc. In both of the first mentioned cases the patients are positive as to its development during the progress of the disease, and while under observation, there has been a slight increase in colour. It will not fail to strike anyone that this deposit of pigment, if further observations /

observations go to support its connection with the other symptoms, is a very important feature, especially as will be shown later on, in view of the fact that the suprarenals may exhibit marked changes. So far, no attention has been paid to this subject. We know that in some cases of Addison's Disease, there may be marked patches of pigmentation as well as the more diffused bronzing so well recognised.

There may be periods now, as in the earlier history of the case, where there is a marked yellow ting-
ing of the skin, quite apart ^{from} the usual dusky lemon tint, these periods corresponding with the exacerbations which still occur. It would seem, however, that this 'jaundice' is less marked in its manifestation than earlier in the history of the case.

Together with this very marked appearance of anaemia there is great debility, loss of muscular energy, incapability of making any effort, or even walking a little fast without great palpitation, and an overpowering sense of fatigue. There may be some oedema of the limbs, but this is seldom the case at this stage. There is now, a constant sensation of weight in the left flank, with dragging. Pain may be severe /

severe, but is not always observed and may be wholly absent from the case. The patient is generally conscious of an increase in size of the abdomen, which does not subside as it may formerly have done.

Temperature.

In this stage we find that the temperature record, which in the early history of the case, may have shown occasional rises corresponding with the slight attacks of the first stage and the more pronounced ones of the first part of the second stage, is now peculiar. The leading character is a high evening rise with a marked sub-normal reading in the morning. The charts in Cases III, VI, XIII, show in some instances an evening temperature of 103° - 104° F. or even higher with a morning drop to normal or lower in many instances. Closer examination, however, shows that, for several days the oscillations may be nearer the normal and less marked; then there may be an evening record of 103° followed by a morning drop, much below what the readings of the previous few days may have been; this may be then followed by a marked sub-normal record for some days with perhaps an evening fall below the morning reading; or again, the temperature may /

may remain for both morning and evening about the same point, this being either about the normal, slightly below or above. In some cases, there may be a gradual increase each evening with a corresponding morning remission closely resembling the temperature chart of typhoid fever. This is very well seen in Case XIII. (Chart p.229 .) These gradual rises may be followed either by a drop to normal, when the cycle recommences, or the temperature may remain elevated for several days and then subside as by lysis.

In fully developed cases I believe these temperature records are the rule, though in Case IV, there does not seem to be any febrile condition. In many cases, especially those in the earlier stages, as I have pointed out, although there may be pyrexia, it is not of high degree, and seems in some instances at any rate to be partly due to slight local peritonitis or pleurisy which, as we shall see, may be a complication. But in the more advanced stages, this high degree of pyrexia is obviously more than can be accounted for by the mere occurrence of local inflammation. This is well illustrated by Case IV., where, although the various pathological conditions are at present in a /

a quiescent stage, there is evidently local peritonitis (perisplenitis) as shown by excessive tenderness on palpation. Again in other cases, vide Cases I, and VI where there was little or no tenderness on manipulating the enlarged spleen, the temperature was, on many occasions greatly elevated. What the significance of this pyrexial condition may be we shall see later.

Alimentary System.

The appetite at this period is variable. It may be fairly good considering the severity of some of the other symptoms; more frequently it is bad, and digestion is also deranged. There are no observations as to the actual condition of digestion as I have been unable to investigate, by means of test breakfasts, in those cases I have seen. This would be interesting in view of the fact that in some other conditions of severe anaemia, pernicious anaemia for instance, gastric digestion has been found in abeyance. Nausea and vomiting may be at times severe, as also diarrhoea. These subside with the other severe symptoms, leaving the patient in the feeble anaemic condition already described.

Physical examination of the system shows some furring /

furring of the tongue, or, if the case be severe, there may be denudation of the epithelium with fissuring, brown coating, etc.

I have not found the lingual follicles increased in size to any abnormal extent as mentioned by Banti.

The teeth, in none of the cases of which records are given, show any syphilitic condition. The tonsils do not show any enlargement except in some few instances where it may have been accidental.

Examination of the abdomen shows more or less enlargement, and possibly, the presence of fluid. This increase in size is most frequently due to the enlargement of the spleen. This organ is found to project far down into the abdominal cavity, forming a more or less oval or oblong tumour, which may fill up the whole of the left side of the abdomen, even extending well to the right of the middle line and down below the level of the anterior superior iliac spine. On palpation there may be great tenderness; in other cases there may be no pain whatever in manipulating the organ. The borders are rounded, and do not, as a rule, give the very definite feeling of the leukaemic spleen; it may be possible to feel one or more notches

The /

The enlargement seems to be general, so that all through the case, the usual shape of the spleen may be retained. It may be found that the spleen becomes much larger, and is then often very tender, this condition lasting for several days at a time, and corresponding with the pyrexial attacks. This relation between the size of the spleen and the temperature is generally best observed in the earlier stages of the disease, for, as already remarked, when this is more advanced, there is less variation in the size of the spleen, and the fever is more constant. Reference to Cases I. and IX. and others, will show that the spleen may, however, undergo marked diminution in size, even ceasing to be palpable below the costal margin (No. I.) Strümpell draws attention to this fact, and there is no doubt that such variation in size is a common occurrence. This fact is therefore at variance with Banti's idea that the splenic tumour is the primary condition, and also with the opinion of Bruhl (No. 13. vol. I. p. 681) who seems to think that the increase in size progresses steadily and suffers no decrease.

Palpation of the spleen may also reveal the presence on the surface of small 'bosses' or local patches of /

of an indefinitely hard character. These are often the most tender spots, and are obviously patches of local perisplenitis. Their presence has often been observed, but their significance is, I think, trivial. Sometimes the most careful examination fails to reveal any. There is often marked increase in the vertical liver dulness (vide figures), but palpation does not reveal any special characters.

Palpation of the abdomen may also show considerable tenderness over different parts of the intestine. This is a point which seems to be passed over in silence by the majority of those who have recorded cases, but is of great importance. As we have already seen, there may be severe diarrhoea and this, with the tenderness on palpation and especially, as I have found, the presence of very dark motions, would all point to intestinal ulceration. That such ulceration does occur is beyond doubt, as will be shown in the chapter on Morbid Anatomy.

The occasional presence of ascitic effusion may mark these abdominal conditions. It often is considerable in amount and may cause great discomfort, especially when there is a large spleen.

The Circulatory System.

The subjective phenomena have already been mentioned.

There may be a certain amount of upward displacement of the heart, the impulse being felt in the fourth left intercostal space; this is evidently due to the presence of the enlarged spleen. There may be more or less dilatation, and soft, blowing murmurs are frequently heard in the different areas. Also in the neck vessels, a venous hum may be heard. The pulse rate presents some curious points; while often being up to 95-100 per minute, it may not show an increase in rate proportionate to the temperature. Thus in Case I., the rate was sometimes 100 or even less, with a temperature of 104° - 105° F. This fact is of interest in reference to the pathology of the disease.

Other heart conditions may be present, but these come under the head of complications.

The Respiratory System.

As a rule examination shows little of note in the system, except, that in many cases, there may be intercurrent pleurisy, as will be described under the head of Complication. It frequently happens that the left base /

base gives an impaired note on percussion from the upward displacement due to the spleen.

The Nervous System.

The derangements of this system are apparently slight and seem to be rather due to the general anaemic condition than to any intrinsic pathological state.

Thus, sleep is fitful, and the patient suffers from great restlessness in the more advanced stages. But as a rule, the nervous complications are unimportant at this stage.

Glandular System.

It is distinctly stated in the accounts of cases of this nature that the lymph glands do not show any enlargement as is found in lymphadenoma. In the case described by Woillez (No.XXII), two in the mesocolon, were somewhat enlarged, but all the others were healthy.

A point must here be borne in mind, that in ulcerative conditions of the intestine the various mesenteric glands may be enlarged, and, as will be seen, such lesions of the intestine are not infrequent, and would probably account for slight increase in size of glands in this position.

In /

In no case, with one exception, has the thyroid been abnormal. The exception was Case VI,) where there was ex-ophthalmic goitre.

Such is the state of the patient in the second stage. This is therefore characterised, at first by the attacks of anaemia, with pain, splenic swelling, etc., being so severe as to lay the patient up, instead of being insignificant as in the first stage; then the general condition of the patient becomes one of marked ill-health with severe anaemia and still the exacerbations of all the symptoms. This stage may last for an uncertain time, varying from some months to several years. It is probable that the cases described by some writers as Banti, Bruhl, etc., have been in this stage more or less advanced, and thus may be explained the discrepancies in some of the accounts, and the short duration accorded to some.

When the period which has been here arbitrarily called the late part of the second stage, is reached, the course becomes rapid, and in a short time, the patient passes into - The Third or Cachectic Stage. Now, there is a great aggravation of all the symptoms: the weakness and debility become so marked that the patient /

patient is confined to bed; the least effort becomes impossible, the patient even being unable to feed himself. Emaciation is rapid, and it may be impossible for food to be retained, so great is the vomiting; diarrhoea may be more or less incessant, and there is usually incontinence of urine and faeces. The patient is drenched with perspirations on falling asleep. The temperature still may show marked irregularity, the pulse becomes irregular, intermittent and feeble. The amaemia becomes profound and the face assumes a leaden grey colour. Bedsores and all the other signs of profound marasmus may appear, with low muttering delirium and the patient soon dies from exhaustion or some intercurrent complication.

Complications.

These are important and often add considerably to the patient's sufferings.

Acute and sub-acute attacks of pleurisy have frequently been noticed, affecting more especially the base of the left lung, and so far as I have seen it is usual to find some evidence of chronic thickening of the pleura. Seeing that there is frequently local inflammation of the splenic capsule, with even adhesion /

adhesion to the diaphragm, this may possibly cause the pleuritis by extension. In some cases pleuritic effusion may be present, and this if considerable, may add to the patient's danger, as it is apt to supervene during an 'attack' when there is already sufficient to cause anxiety. Other pulmonary complications are oedema and an asthenic form of pneumonia, which occurs more particularly in the marasmic stage, and is frequently the direct cause of death.

The heart may be affected organically, for endocarditis has been observed in some cases, and found to be recent post mortem. (Williamson No.17). Chronic endocardial murmurs have been present in two of my own cases. There is generally cardiac dilatation in the later stages. Pericarditis has not been noticed in any cases so far as I know. Effusion of fluid into the peritoneal cavity is not infrequent. In one of my cases, (No.II), it formed a constant feature of the 'attacks' and is one of the things the patient notices when he feels he is becoming weak. In this case it does not reach to any great extent and generally disappears of its own accord, although in this particular instance tapping was tried. It is not exactly clear what /

what its cause may be, for it does not seem to be peculiar to cases in which the spleen is very large. The changes in the liver may have some influence on it.

General peritonitis has been observed in some cases (Williamson op.cit.Müller, No.34), and was found to be due to perforation of intestinal ulcers, themselves a complication in many instances. They were present in Case No.I., as will be shown below. The occurrence of local peritonitis (perisplenitis) does not need further mention.

Nephritis may be a serious complication, notwithstanding Banti's assertion that it does not occur.

The nervous system does not usually present any complications except those incident to anaemia and the general asthenic state. In Case I., there were convulsive seizures on two occasions, but it is difficult to say how these may have been caused, for in this instance there was considerable nephritis (though not copious albuminuria.)

Graves' disease was present in one of my own cases (No.VI.)

Haemorrhages may be looked upon as a complication especially when severe.

Epistaxis, /

Epistaxis, haemoptysis, haematemesis, and intestinal bleeding have all been noticed, and may be in some cases alarming. The first, especially, has often been present to a severe degree.

Purpuric eruptions have been recorded by Bruhl; they formed a marked feature in my own case, No. III.

A curious complication in Case VI., was an attack of measles which the patient developed while in hospital. The attack showed nothing peculiar in itself but was followed by an alteration in the temperature, for, from being very irregular, with marked remissions, it became for a considerable period very much steadier, rarely showing any elevation above 99° . This continued till the patient developed what was thought to be a slight attack of erysipelas; the temperature after this, resumed its previous characters.

Vide Chart p. 211 .

CHAPTER IV.

THE BLOOD.

The examination of the blood in this disease, presenting as it does, anaemia as one of its most striking features, is of extreme importance; such examination reveals some very characteristic conditions.

In all the cases which have come under my own observation, I have examined the blood both quantitatively and qualitatively, using the various modern methods of investigation, such as differential staining, etc. The conditions found in the blood are as follows :

- (a) Oligocythaemia.
- (b) Absence of Leucocytosis.
- (c) Variation from the normal amount of haemoglobin.
- (d) Presence of abnormal and deformed elements in the blood.
- (e) Variation in the chemical constitution.

(a) Oligocythaemia, or reduction in the number of corpuscles is found in all cases, and may be a very early symptom. It is, as a rule, progressive, although it may, for a time, especially in the first stages /

stages, become stationary. There may even be in some cases an increase in the number of corpuscles, especially when the patient comes under treatment; still the amount of improvement is slight, and any untoward circumstance, however trivial, would seem to at once cause a fall in the number of red cells.

As would be expected, the cases in which the reduction in the number of the corpuscles becomes arrested are those which have begun with less pronounced symptoms, and which are evidently of a more chronic type. In others, where the decrease is from the first, marked, and the general symptoms severe, it is doubtful if any true improvement in the oligocythaemic state takes place. Thus, in the case of A.S., (No. III), although there was some fluctuation at times, the decrease was progressive. So far as I can find, the amount of increase, even in the apparently slow cases is generally within 500,000, or, in other words, the amount of increase is much less marked than the decrease when such occurs; again in a very short time the corpuscles may make a considerable drop, while it takes several days to make a partial recovery.

The following figures give the estimations
in /

in some of the cases already quoted:

Case VII. A.P., March 1892,	R.B.C.	=	3,820,000
	W.B.C.	=	12,000
	Haemoglobin	=	50 per cent.
Oct. 1892,	R.B.C.	=	3,300,000
	W.B.C.	=	16,000
	Haemoglobin	=	60 per cent.

In this case, the disease is now of some duration, (vide.p.212), but the patient has not become cachectic, and it seems to be at this period that the fluctuations in the corpuscular numbers are most evident.

In Case II, the numbers were:

Sept 10th,1893	R.B.C.	=	3,650,000
	W.B.C.	=	10,000
	Haemoglobin	=	30 per cent.

Sept 30th after an attack :

R.B.C.	=	3,200,000
Haemoglobin	=	23 per cent.

Oct 21st	R.B.C.	=	3,340,000
	Haemoglobin	=	25 per cent.

Jan 13th,1894	R.B.C.	=	3,520,000.
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The patient is now feeling much better.

As a contrast to these figures, it may be shown what they may fall to in the more rapid stages.

Thus, /

Thus in Case I, when first estimated:

Feb. 1893, the R.B.C. = 3,670,000

On Oct. 18th, I found:

R.B.C. = 2,130,000
W.B.C. = 15,000
Haemoglobin = 10 per cent.

On Oct. 25th, a few days before death, I found:

R.B.C. = 1,620,000
Haemoglobin = 10 per cent.

Even in cases where, to all appearances, the patient seems quite well there may be a fairly marked oligocythaemia; thus in the case of Alice P., (No.VIII), the number of corpuscles was:

R.B.C. = 3,800,000
W.B.C. = 20,000
Haemoglobin = 60 per cent.

Here, unless attention had been directed to the patient from a knowledge of the hereditary condition, this blood state would not have attracted much attention. Other figures are given in the accounts of the cases (vide infra).

These figures show clearly, I think, the constancy of this reduction in the number of the red corpuscles. The lowest numeration I can find recorded is in a case noted by Landouzy (No.XXI) where Malassez /

Malassez, by whom the examination was made, found only 1,000,000 R.B.C., the proportion of white being 1-312; in this case, however, there had been severe epistaxis. The next lowest figure, is, I believe, in my own case (No.I) where as already stated, the R.B.C. about 5 days before death were only 1,620,000.

(b) Absence of increased white corpuscles. The white corpuscles do not show any increase in their number as a rule, thus, taking 10,000 per cubic millimeter as the average in health, we find that this figure is pretty constantly maintained, the variations not being more than can be accounted for under ordinary conditions. Thus, in the case of Alice P., (No.VIII) the number given is 20,000, but we must bear in mind the age and sex of the patient. I have, on other occasions too, found 20,000 or even 30,000 white cells present, but this would seem to be merely a leucocytosis, for as we now know, a slight increase in the number of these cells is of frequent occurrence, but does not constitute leucocythaemia, or even a tendency to it. In that disease the essential feature is the presence in the blood of abnormal forms /

forms of leucocytes, (Stanley⁽²⁵⁾); and unless we find this to be the case, we are not justified in considering a somewhat increased number as having any relation to leucocythaemia. Now in all the cases under consideration, I have paid careful attention to this point, and have never found any but the usual forms of white corpuscles. There are the tri- and mono-nuclear cells with a few eosinophilous cells, which latter were always of the usual size, and bore the average relation to the total number of white corpuscles (2% to 3%). From these facts, I think we may look upon the condition of the white cells as normal, and in all cases, where the estimations have been carefully made, the evidence is all in favour of the white cells being unaffected. It is, therefore, difficult to understand Banti's statement that he considers an augmentation, more or less marked of the leucocytes to be the rule. Nor do his own figures support this supposition, for, although he gives the numerical condition of the blood in his Case No. I[§] as:

R.B.C.	=	3,751,000
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W.B.C.	=	34,000
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this can be easily accounted for by the fact that the /

§ Banti, No.12, p.67.

the patient was at the time suffering from pneumonia; thus the apparent increase was really a symptomatic leucocytosis. In his other cases Nos. 2 and 3, he gives the number of white corpuscles as 4,704, and 6,876 per mm³ respectively. It would seem, therefore, that this author's conclusions as to the increased number of white cells is not based on accurate facts.

An important point in the examination of the white corpuscles has been to see if any of them contained pigment granules. In all the cases I have examined, on no occasion have the white corpuscles contained pigment. The point is an important one, and with the exception of Banti, no writer so far as I can ascertain, has noted the fact.

(c) Variation from the normal amount of haemoglobin. In all cases, there is a reduction more or less of haemoglobin, the various figures being already given.

At the same time, it would appear that the reduction in haemoglobin is much more irregular than that of the red corpuscles within certain limits, even in some instances not being in the same proportion. Thus, /

Thus, in the case already quoted (No.VII) the haemoglobin had actually increased, while the number of red corpuscles had decreased. I have observed this on other occasions and, especially in Case No.IV, careful estimations were made as to the point; thus on one occasion the relative figures were :

R.B.C. = 3,100,000

Haemoglobin = 30 per cent,

while about a fortnight later they were :

R.B.C. = 3,220,000

Haemoglobin = 50 per cent.

It is evident that in some cases, therefore, we have a high proportion of haemoglobin as compared with the number of red corpuscles, thus calling to mind the same condition found in pernicious anaemia. Towards the end of the cases, so far as I can find, there is a greater fall in the amount of haemoglobin, for in Case No.I, the reading was 10%, R.B.C. being 1,620,000.

Further remarks will be made in the consideration of the pathology. It must be stated at the same time, that the readings, given above were obtained with Gower's Haemoglobinometer; with the Haematoscope of Hénocque, much higher readings were given. However, as /

as my earlier observations were made with Gower¹⁸'s, I have thought it best to keep to this for the sake of a standard.

So far as the coloration of the corpuscles is concerned, it may be frequently observed, especially in the more advanced cases, that they vary much in tint, some apparently containing much more haemoglobin than others, and in a few the haemoglobin appears in masses.

(d) The presence in the blood of abnormal and deformed elements.

The examination of individual blood cells shows changes from the normal in the majority of cases, though in a few, there seems to be little variation. As in so many other points, so in the blood these changes vary with the intensity of the disease so to speak, and probably with its duration. The most constant change found is a variation in size of the red corpuscles, there being usually, or I may say constantly a considerable number of these which measure only 4 - 5 μ in diameter, some even less; but, speaking generally these smaller corpuscles vary between 5 and 7 μ , during the early stages, while in the later or /

or at the time of an exacerbation, greater differences are found. Banti, Brühl and others have also remarked this fact. In some cases I have found red cells very much above the average in size, having a diameter of 10 μ . With the exception of a passing remark by Williamson (No.17) no mention has been made of this fact, so far as I can find, and it is somewhat surprising that Banti (No.12) does not appear to have observed them.

It is often stated that there are no poikilocytes present in the blood (No.15). That this is true to some extent there can be no doubt, but it has been a distinct feature in two of my cases (Nos.III & VI), and in one of those recorded by Williamson (No.XIII), a considerable number were seen. This is not, however, a constant character of the blood, and may disappear entirely for a time; this would perhaps account for its not being mentioned by some writers. When present, they are seen under similar circumstances as the smaller blood cells just mentioned, sometimes disappearing for a time. In Case III., they were present in great numbers when the patient first came under observation, and then gradually decreased till only one or two could /

could be seen in the field. It is common, however, for many of the coloured cells to show an oval form, and this is much more constant than the presence of pear-shaped or flask-like cells. A curious fact, and one for which I am not at present prepared to offer any explanation, was, that in Case I., I never found any poikilocytes notwithstanding the profound anaemia, (vide pp.178-81): they were most carefully looked for, the blood being examined under many conditions. We may, therefore, say that, while some cases show little change in the shape of the red corpuscles, these may, in others show all the various forms observed in circumstances of severe anaemia. Also it may be seen that the definite statement of Labadie Lagrave (op.cit) that the shape of the red cells is generally retained and that poikilocytosis has not been observed, is one not supported by facts.

In all cases I have made careful search for the presence of nucleated red corpuscles and found them on one occasion in Case III. It might appear surprising at first sight that in cases showing very severe anaemia, they should be absent as a rule, but this is not peculiar to the disease under consideration for Quincke (No.26) failed to find any in a long /

long series of observations on pernicious anaemia. Further reference will be made to this fact when considering the pathological conditions. On several occasions I have found small corpuscles measuring 2 - 3 μ , globular in form and showing a distinct yellow red colour; these are quite distinct from the small red corpuscles already described, for these latter, though relatively small, are somewhat larger, are not globular, and show variation in shape. It will be seen at once that the description of the former corresponds with that given by Eichorst (27) of certain cells found in the blood in pernicious anaemia. This writer considered them to be pathognomonic of that disease, but they have been observed under other circumstances. As in pernicious anaemia, they varied in their presence. I often failed to see any at one examination and then found them the next day. As to their nature, it is not possible to say much here, but perhaps some important evidence may be obtained in support of their being of destructive origin, by the fact that they were most frequent in Case III at the time that the greatest number of poikilocytes were present and that I was sometimes enabled /

enabled to watch the fragmentation of these latter, the processes becoming broken off, contracting to some extent, and finally assuming a perfectly spherical form, having a diameter equal to that given above. I believe that these small bodies then become stained with haemoglobin which they may absorb in some manner. The other case in which I found them was (4^{VI}) in which, as already stated, the anaemia was profound. I look upon their presence in the blood in these cases as a very important point, the significance of which will be shown later. Regarding the blood platelets, I have not observed any pathological variations.

(e) Variation in the chemical composition.

Lastly, in those cases where the anaemia was most marked there was reduction in the specific gravity of the blood, but I have been unable to obtain sufficiently accurate results, to state the amount of deviation.

The coagulability is also much delayed, and a marked reduction in the alkalinity of the blood was a feature in some of my cases, and in Case XXV, it was acid.

It may be well to sum up briefly the blood changes thus /

thus described, as they are of great importance. A reduction more or less marked of the red corpuscles is a constant characteristic and exists from the earliest stages; this reduction is more marked when there are exacerbations. During the intervals the number of red corpuscles may be increased but this takes place slowly; during the later stages the reduction is progressive and may exceed 80% of the normal. The white cells may show no deviation either quantitatively or qualitatively from the normal, any temporary increase being only such as may occur physiologically. The haemoglobin is reduced in amount, but not (in some cases and in early stages) proportionately to the oligocythaemia. In the ~~marasmic~~ marasmic stage, the reduction of haemoglobin may be extreme.

Except in the early periods of a disease, a variation in size of the red corpuscles is a fairly constant feature, while in the later it is the invariable rule; the corpuscles may show slight tendency to the oval; poikilocytosis may be observed, and may even be marked; but is not always present and may disappear altogether for a time; it probably is related to the amount of anaemia; large red blood /

blood cells may be present; nucleated red blood cells have been observed; also 'Eichorst's corpuscles'. The blood platelets appear normal (?). There may be changes in the specific gravity, reaction, etc.

It only remains to say that the blood has been examined for the presence of micro-organisms, plasmodia, etc., but with negative results.

CHAPTER V.

THE URINE and FAECES.

The Urine.

Very little attention has been paid to the characters of the urine in splenic anaemia by any of those writers who have recorded cases, and judging from my own experience the few observations recorded seem to be inaccurate. In the most recent account of the disease, that by Labadie-Lagrave (15) he dismisses the whole subject in four lines, saying that the quantity varies, and that there is nothing constant to be noticed in the urine. Banti (12) gives very little more information. Bruhl (13) certainly notices the fact that the urine may be very dark coloured giving a rose colour with nitric acid.

There can be no doubt in view of recent work on the characters of the urine in certain conditions of anaemia, especially the observations of Hunter (28) that careful and complete examinations are of primary importance. Doubtless, had the writers named done so, they would have found indications of the probable pathology of the disease.

The quantity is certainly variable, and does not seem /

seem to follow any particular condition, except that in the later stages it becomes reduced. This is in part due to the frequently accompanying diarrhoea. The only point of importance so far as the quantity of urine is concerned is that it may amount to 1450 cc or 1550 cc while still presenting a high colour.

The most important feature, and one which is almost constantly observed is the peculiar colour of the urine, this being of a red-yellow, or deep red orange. This is not always of the same intensity and when speaking of it as a constant feature, I do not mean that the urine is always so coloured, but that in every case, so far as I can find, this deep coloration is present at some time or other: it may at times completely disappear, the urine then being quite pale. This character early attracted attention in the cases described by Dr Claude Wilson, and subsequently by the same writer and myself conjointly (16). Since then, I have never failed to find it in all my own cases, with one exception; here, however, I shall be able to show that this is more apparent than real. In some cases (e.g., Nos. II and IV.) I have not even found the intermittence of deep colour just mentioned, the urine, being /

being always, so far as several months of observation go, of a deep yellow or red-brown yellow, with a specific gravity not above the average and no abnormal decrease in quantity. In Case IV., this was especially the case; here also there was no febrile condition as is so often observed, and which may cause the usual characters of the urine in such states to mask the appearance peculiar to this disease. The most usual thing, however, is the intermittent coloration, and this condition varies with the same intermittence of all the acute symptoms, as already described. Therefore we find that with the attacks, there is the passage of urine of this deep colour; when the attack subsides there is a return to a less marked tint or even a pale urine. Consequently, we must look upon the peculiar coloration of the urine, whether constant or intermittent, as the indication of some peculiar pathological process.

It, therefore, became of importance to discover to what this coloration was due; to this end careful spectroscopic examination of the urine was made in ^{every} _A case, except two (Nos.V. and XII) as the patients had died before the investigation of the urinary pigments was /

was begun.

In a specimen from Case VII, obtained during a typical attack and showing the characteristic orange-red-brown coloration, the urine without any treatment showed an intense black band at the blue end of the green and on diluting with water the band became more distinct reading as follows for the wave length - $\lambda 501$ to $\lambda 469$. In the deeper layer of the urine no other bands were visible. In a tolerably deep layer of an acidulated alcoholic extract, there was a faint shading visible before D., and a band in the green, with ill-defined edges. On diluting with spirit., the band in the green was seen to extend from $\lambda 569$ to $\lambda 535$, and now, an intensely black band was visible in the blue end of green, with the edge towards red, better defined than that towards violet, the latter being the less deeply shaded. On diluting still more with spirit, the band at the blue end of green was found to extend from $\lambda 511$ to $\lambda 483$.

It will be seen from this examination that the coloration of the urine was due to the presence of pathological urobilin in large quantity.

These highly coloured urines were also examined for /

for the presence of urohaematoporphyrin, and though in one case, the absorption bands were slightly suggestive of its presence, the others gave no indication of its forming a factor of any importance as a pigment, while in one case it appeared to be distinctly present; this fact was of much importance as bearing on the influence of the suprarenals. (vide infra p.147)

Uroerythrin appeared in considerable amount, in the febrile urine of the pyrexia attacks.

Reaction.

The reaction of the urine was generally acid, often markedly so, especially during the febrile periods, but in Case III, it frequently showed a neutral or feebly alkaline reaction.

Specific Gravity.

The only point of importance in this connection was the one already mentioned in speaking of the high colour, viz., that there was no corresponding rise in the specific gravity. It, of course, showed the usual change in relation to temperature, when this was elevated, but at other times when the temperature was normal or subnormal the specific gravity ranged from 1010 /

1010 to 1015, showing that the high colour was independent of concentration.

Urea.

This substance generally appears diminished in amount, the quantity often being as low as 12 grms, (normal average = 38.1 grm.) and even in the presence of pyrexia I believe it is under the average, judging from the estimations I have made; on the other hand it is not unfrequently over the average, the extreme given by Labadie-Lagrave being 11 grms - 45 grms. All that can be said therefore is that the amount of urea excreted varies considerably, but that the tendency is for a low total. Mosler (29) states that the quantity of uric acid is also diminished; on this subject I have no statement to make.

Phosphoric Acid.

Several estimations have been made in Cases Nos. III, IV, VI, etc., and the results have shown a considerable reduction in the excretion. Taking the mean as 3.42 grms (30) the estimations in these cases varied between 0.525 grm and 2.17 grm.

Chlorides generally showed some corresponding reduction.

The /

The sulphates have given varied results, but do not seem to be much affected.

Albumen.

Albuminuria is of frequent occurrence, but may be intermittent. In Cases III and IV it was present on all occasions, while in Case VII it was intermittent. And here I have to differ from the statement of Banti (12) (p.97) that albumen is never found, although he admits that it may be present in traces in the latter stages of cachexia. Labadie-Lagrave (15) (p.318) makes a similar assertion copied apparently from the former author. Having now observed cases in all stages, I can say that while many of those in the later and marasmatic, frequently show a considerable amount of albumen, others in a much earlier, may have it intermittently. Some cases prove exceptions, e.g., Nos.V and XI, in neither of which did the urine give reactions for albumen. Therefore, Banti's statement is much too absolute. The question is an important one as I shall show in speaking of the pathological anatomy (p.90).

Bile Pigments.

On some occasions a slight reaction for bile pigments /

pigments was obtained but not constantly and it is important to remark that this seemed quite independent of the high colour of the urine, for as a rule, no bile reaction was obtained, even when the coloration was deepest. No reaction for sugar has been found in any of the cases of which records are given.

Indoxyl-sulphate of potass (Indican) has sometimes given reactions, but I have not been able to get any result in any of my own cases. Peptones have not been found.

An important point is, that no haemoglobin reactions were obtained in any of the cases where I have been able to examine the urine. Methaemoglobin was, however, present in one case (No.XV) as well as urobilin. This absence of haemoglobin marks these cases off distinctly from other conditions where haemoglobinuria is observed (vide p.135).

Microscopic examination has shown the presence of casts in some cases, but the most interesting point is that, in Case III., I detected cells, evidently of renal origin which contained pigment granules. Similar cells have been observed by Hunter (28) (p.328) in a case of pernicious anaemia. In reference to Case /

Case XV also it is stated (19) that the urine contained 'material resembling broken-down blood corpuscles'.

It will be seen from a consideration of the urinary conditions therefore, that important information may be gained from its examination; what the pathology of it may be I shall give later.

The Faeces.

Little can be said on the subject of the faeces, but one or two important facts may be noticed. In Case IV they were sometimes black, while the patient James K., (No.II), said that he passed some blood with the motions. As will be seen further on, ulcerative conditions of the stomach and intestine may perhaps account for this; but still the dark colour of the faeces, even when the jaundice was very marked, is an important point. In Case.I., they were of a dark slate grey colour.

CHAPTER VI.

AGE OF ONSET - DURATION.

As we have seen above, the onset of the disease is extremely vague and insidious. On this account, it is extremely difficult, and, in many cases, impossible to ascertain with any certainty, the age of onset, and therefore the duration.

In Table [^] an attempt is made to state the age when the case first came under observation, the diagnosis of an enlarged spleen or else some prominent symptom as epistaxis, with asthenia, being taken as a guide. If we refer to the works on diseases of children, as quoted above, we find the onset may occur at a very early age. Here however, we are at once met with the difficulty, that many cases of enlarged spleen, other than those under consideration, are included. Among the earliest cases I can find, are those recorded by Dr Wilson and myself, where there was definite evidence of splenic disease in the first years of life; in the case of Mrs B. (No. IV) her only child died at the age of 5 months, and the medical man who attended informs me that there was great enlargement of the spleen. In referring to Table [^], we see that /

that the age of onset is variable, and not by any means confined to children, for cases are there shown where the history pointed to an onset as late as 71, and there are several between 45 and 55. The number of cases here recorded is far too small to be conclusive, but comparing these figures and those of other authors, it would seem as if the disease may occur at any age, and is not, as some would seem to think, more frequent in childhood, an opinion which is most certainly inaccurate.

Duration.

The duration of splenic anaemia has been variously stated by different authors. Strümpell⁽²³⁾ gives 2-3 years, Müller (3) says it may last over four. It would seem, however, that the figures fall far short of being accurate. It is true that many cases do not last longer than stated by these authors, but this may often be due to the fact that the disease may run a latent course for several years without attention being called to the condition. Thus, in the cases of Alice P., and her two cousins (Nos.VIII-X) the patients appear fairly healthy, and enjoy good health, and were it not that the existence of enlarged spleens was known/

known to prevail in the family, these cases would escape observation till such time as they begin to suffer from profound anaemia. In the cases (Nos. XI & XII) recorded by Dr Wilson and myself there is distinct evidence of a duration of over 30 years. In one of my own cases (No. 1) there is reason to believe the duration to have been over 18 years, and in another (IV) there is the evidence of the patient's doctor to show she has suffered from an enlarged spleen for over eleven years. In Case (No. II) I believe that the history extends over 14 years, but it is not possible to make certain.

We may gather therefore, that while many cases seem to run a more rapid course, others may last several years without greatly interfering with the patient's comfort.

Sex.

There seems to be a greater tendency in the male sex to suffer from splenic anaemia. Thus, of the twenty-eight cases given in Table , sixteen were males and twelve females, which shows a slightly greater preponderance of the former. The number is however, too small to allow us to state definitely what the relation may be.

CHAPTER VII.

MORBID ANATOMY and PATHOLOGY.

Autopsies have been made in several cases by Continental observers, but, as a rule, the accounts given are incomplete. In English medical literature there is still less to be found, and, in the majority of cases, the spleen only is described, any other tissues being passed over, so that probably many of what may possibly be the most important lesions, are undescribed. So far, the best account in English is that of Case XIII, by Williamson (17). I have been enabled to examine two cases myself, the first, (in order of time) being Case No. XII, the second is that which is described clinically as No. I.

The first of these, XII has already been briefly recorded (16) but the latter is given here for the first time.

I shall give first an account of the pathological appearances observed in these two cases § , and then refer to those found by others.

§ Unfortunately a complete examination could not be made in either case owing to the relatives.

CASE XII. (Vide p.222 for clinical account).

Autopsy about five hours after death.

Body not emaciated.

Peritoneum healthy; no effusion, or any appearance of peritonitis. The uterus was firmly contracted.

The liver was decidedly enlarged, projecting beyond the costal margin for nearly two inches, the left lobe ^{extending} to the ribs of left side, and somewhat depressing the spleen. The organ itself was firm, smooth and somewhat pale in colour. The spleen was much enlarged, weighing almost 32 ozs, measuring $6\frac{1}{2}$ x 5 inches, and being 12 inches in circumference at the middle. This enlargement was symmetrical, the shape being preserved. The organ was extremely firm and of a dark, purple red; the capsule greatly thickened and presenting at the upper extremity of the organ, a large cartilaginous patch of old perisplenitis. There had been no adhesions to any other organ. On section, it was firm and dark red, the capsule showing much thickening, and from it, trabeculae, also greatly thickened, extended through the spleen substance. There were no infarcts to be found, and the Malpighian corpuscles were not prominent, being apparently smaller than usual /

usual in many parts of the cut surface. There was nothing resembling the "suet-like" appearance of these, as seen in lymphadenoma.

The kidneys appeared normal in size and colour, the capsule stripped, leaving a finely irregular surface.

The pancreas was not enlarged, but very tough, feeling almost gritty.

No enlarged lymph glands were found anywhere.

No other organs could be examined.

Microscopic Appearances.

Spleen. There is great thickening of the capsule and trabeculae; these latter being especially distinct towards the periphery of the organ as they pass from the capsule. Here and there, are irregular patches consisting almost entirely of red blood corpuscles crowded together, evidently small haemorrhages. Everywhere the meshes of the reticulum appear more distinctly than normal, as if there were a general increase in the fibrous tissue. Some of the venous sinuses are somewhat dilated.

Several apparently normal Malpighian corpuscles are to be seen, but not so many as in a normal spleen, while several appear to be undergoing a process of sclerosis /

PLATE III.

Fig.1. - Spleen. x 900.

- (a) Arteriole in the centre of a fibrous Malpighian corpuscle undergoing fibrous thickening.

Haematox. and Eosin,
Case XII., vide p.73.

Fig.2. - Spleen. x 900.

- (a) Malpighian corpuscle converted into a knot of fibrous tissue;
(b) invasion of splenic reticulum adjacent to (a) by fibrous tissue.

Haematox. and Eosin,
Case XII., vide p.73.

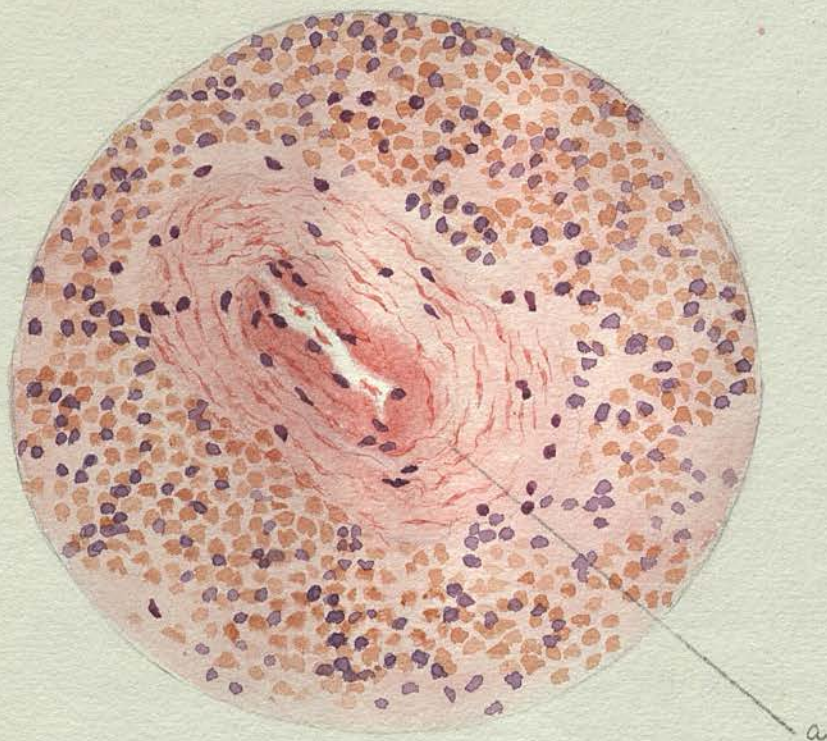


Fig 1

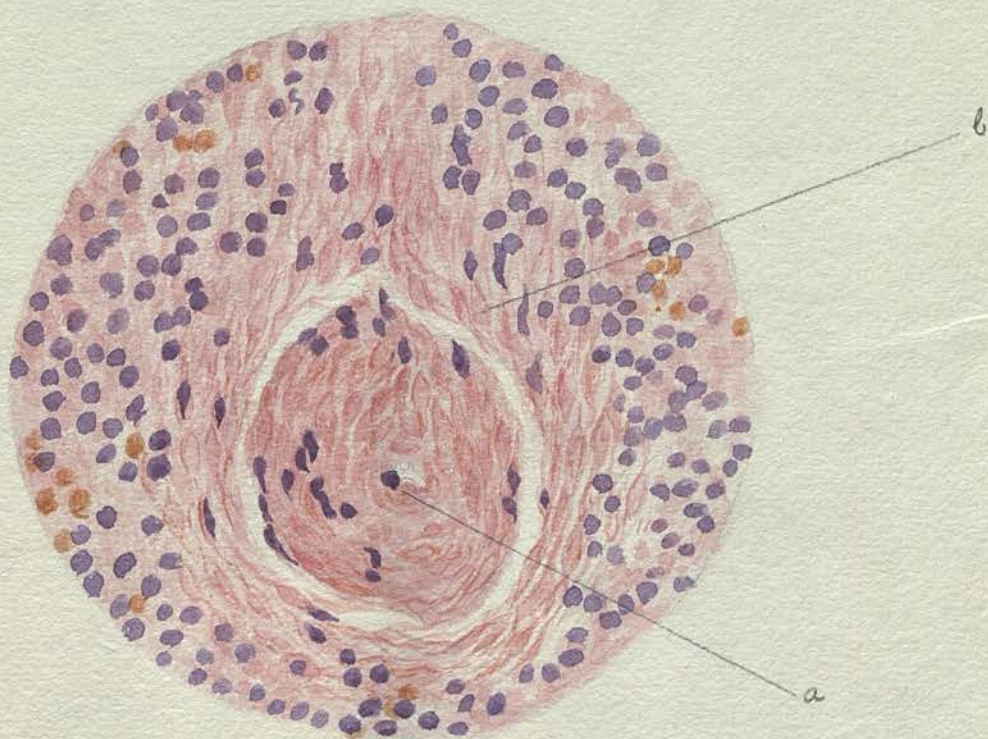


Fig 2

sclerosis. The central arteriole, in these cases where the process is in an early stage, shows thickening of its walls with diminution of its lumen; (v. Plate III, fig.1), while the perivascular tissue seems to have increased in amount, and the lymphoid cells to have partially disappeared. In a further stage the corpuscle and vessel may be seen to be converted into a mass of fibrous tissue, the latter showing no lumen or only a trace of one (Plate III, fig.2), the whole structure then apparently undergoing contraction, while the connective tissue round it undergoes further increase. In some parts of the section, this gradual invasion of the lymphoid tissue or its transformation into connective tissue is very well seen and is represented in Plate IV, fig.2, where the connective tissue fibres may be seen working in between the lymphoid cells, which come to be arranged in parallel lines, then seeming to disappear.

There is, in this spleen, no deposit of pigment round these altered Malpighian bodies, but here and there through the section small masses may be seen occupying different positions, but frequently lying in the spaces between the connective tissue fibres (Pl.IV.fig.1.)

The /

PLATE IV.

Fig.1. - Spleen. x 900.

- (a) at the margin of one of the trabeculae,
showing its encroachment into the
splenic reticulum
- (b) from which the lymphoid cells are dis-
appearing;
- (c) small deposit of haemic pigment in the
strands of fibrous tissue.

Haematox. and Eosin,
Case XII., v.p.73.

Fig.2. - Spleen. x 650.

- showing the invasion of the reticulum by
the periarterial fibrous tissue;
- (d) thickened wall of vessel;
- (e) advancing fibrosis, the lymphoid cells
becoming placed in parallel rows;
- (f) at the margin of the adenoid sheath.

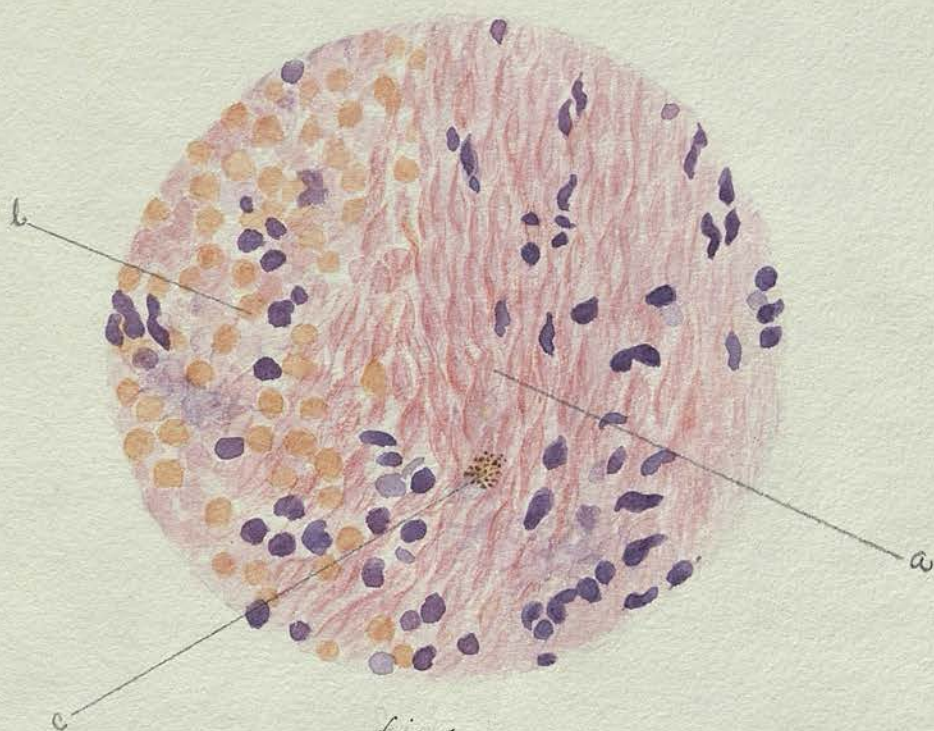


Fig 1

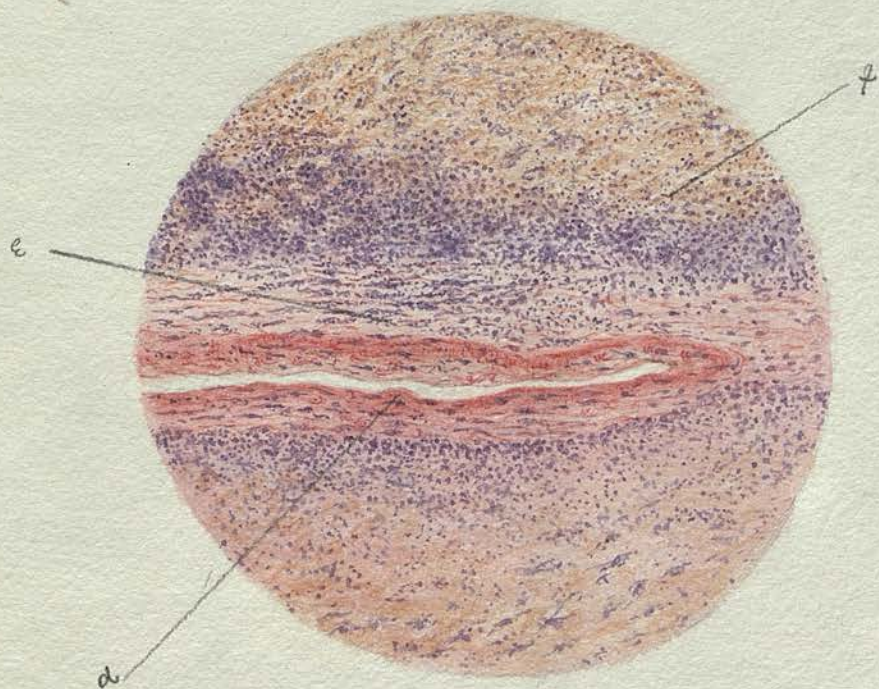


Fig 2

The same process of fibrous tissue invasion may be frequently seen at the borders of sections through the trabeculae, and is shown in Plate IV, fig.1, which represents part of the splenic reticulum close to a thickened trabecula; the fibres of which may here be seen passing into the neighbouring tissue, with disappearance of the lymphoid cells.

Liver. The lobules are not mapped out distinctly nor is there any apparent increase of connective tissue, except to a slight degree in some of the portal spaces where the perivascular tissue seems in some excess, but there is no abnormality of the bile ducts; the intra-lobular capillaries are much dilated (vide, Plate V, fig.1.). In a considerable number of the liver cells are fat globules and the majority of those not so altered, contain a large quantity of golden-brown pigment, while in many instances the cells contain both fat and pigment. When the sections of liver are treated with a solution of potassium ferrocyanide and then passed through a weak solution of hydrochloric acid (No.31), this pigment becomes quite blue. The explanation of this will be given later. The pigment is distinctly within the liver cells (Plate /

PLATE V.

Fig.1. - Liver. x 900.

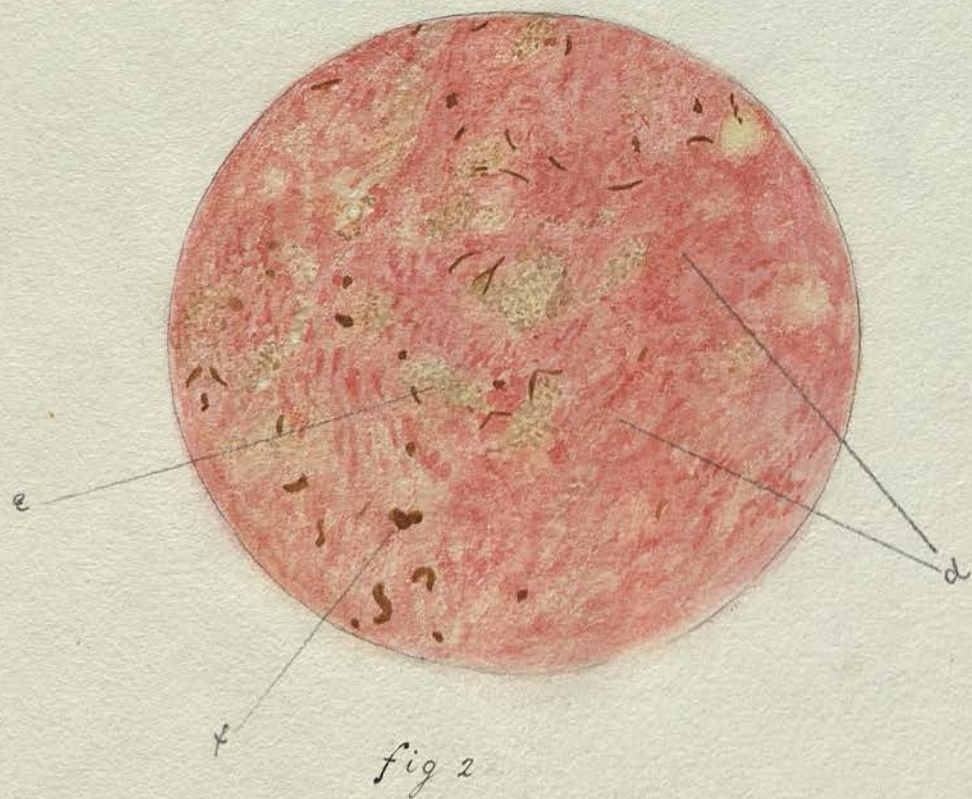
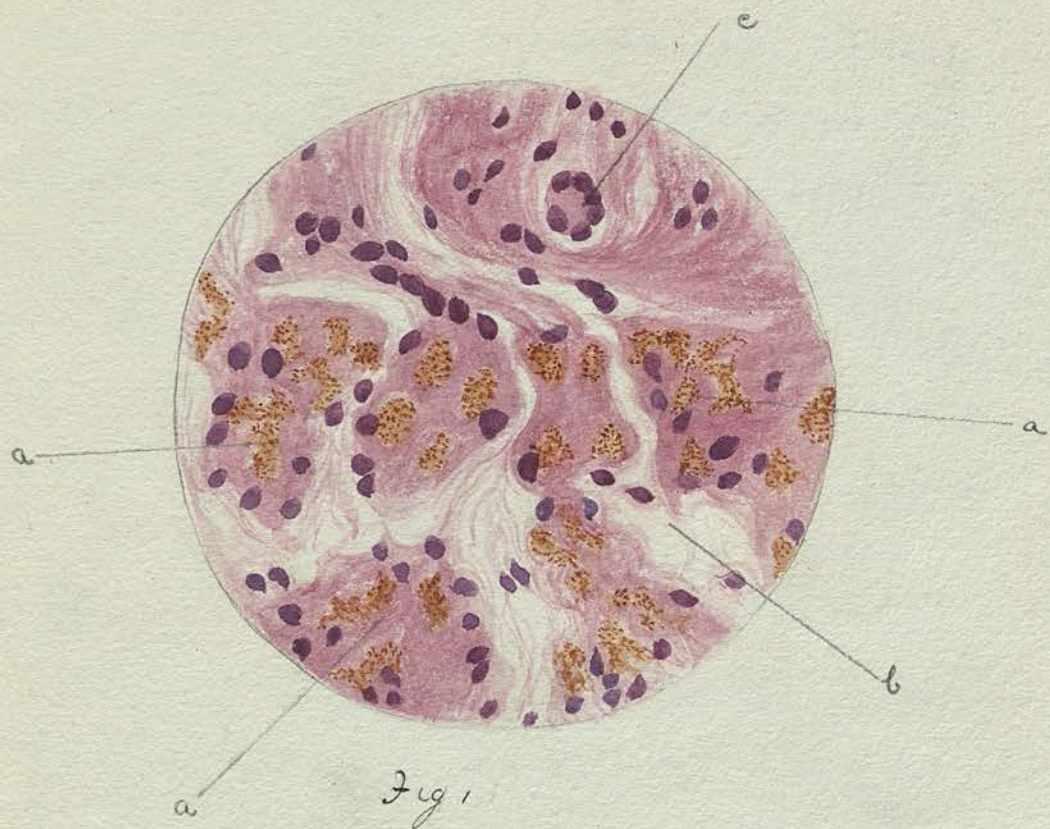
- (a) Liver cells containing pigment of haemic origin;
- (b) dilated capillaries;
- (c) bile vessel unaltered.

Haematox. and Eosin, vide p.77.

Fig.2. - Suprarenal Body. x 600.

- (d) fibrous tissue;
- (e) remains of glandular cells;
- (f) small blood vessels.

Picro-carmin, vide p.88.



(Plate V, fig.1.), often surrounding the nucleus, and the cells which contain the greatest quantity of pigment are those in the outer two-thirds of the lobule, while nearer the central zone, the fatty changes are more marked. Here and there a few granules of pigment may be seen, apparently free in lymph-spaces, but this is exceptional.

Nowhere in the liver is any lymphoid growth to be seen.

Pancreas. Everywhere throughout the section, there is to be seen increase of interstitial tissue, but this condition is much more marked in some places than in others; there is also increase of fibrous tissue in the interlobular spaces; the periacinar lymph spaces are somewhat dilated. The glandular epithelium itself appears perfectly healthy. (Plate VI, fig.2.).

Kidney. There are patches of fibrous tissue to be seen throughout the section, especially in the neighbourhood of the capsules of Bowman: these latter are markedly thickened in some places, and from them the interstitial tissue passes in between the convoluted tubules. The excretory epithelium shows evidence /

evidence of desquamation, and in the cells of the convoluted tubules, distinct pigment granules may be sometimes seen (Plate VII, fig.1). This pigment gives the same blue reaction with ferrocyanide of potassium and hydrochloric acid as described above. It is only in this situation that the pigment may be seen, none being found inside the Malpighian bodies. The arterioles show considerable thickening of their coats. The changes in the kidney, therefore, consist in a somewhat generalised interstitial nephritis.

Lymph glands. One examined microscopically appears quite healthy.

The second Case on which I was enabled to make a post-mortem examination was No.I. The conditions were as follows: (Abdomen only could be examined). The body was very emaciated, rigor mortis passing off, lividity slight. The peritoneum appeared healthy.

The spleen was much enlarged, weighing about $2\frac{1}{2}$ lbs; it did not present any adhesion and was of the usual shape, notwithstanding the size. It was very firm, and of a dark red colour. There were no local patches of perisplenitis found. On section, it cut with a well-defined margin, and was of a dark red colour. Here and there, especially in the region of the /

PLATE VI.

Fig.1. - Suprarenal. x $2\frac{1}{2}$.

- (a) cyst in the lower portion of the organ;
- (b) cyst wall formed by medullary portion;
- (c) upper part of the organ showing very slight increase in fibrous tissue.

Celloidin, Haematox. and Eosin;
Case I., also p.88.

Fig.2. - Pancreas. x 800.

- (a) marginal portion of lobule becoming invaded by fibrous tissue;
- (b) unaffected central part of lobule;

Haematox. and Eosin,
Case XII., vide also p.77.

the hilus, were areas which were more dense than the rest of the organ, and paler, being apparently more fibrous than the rest. The trabeculae were everywhere thickened, and the Malpighian corpuscles were seemingly much diminished and fibrous in many cases, but unaffected in others. There was no appearance of infarction.

Liver. This organ was enlarged, smooth, pale, and on section the lobules appeared distinctly marked out as by fatty changes; there was no distinct naked-eye appearance of cirrhosis.

Suprarenals. The left suprarenal was small, very firm and appeared more surrounded with connective tissue than usual.

The right was considerably larger than the left, and while presenting the usual naked-eye characters in its upper portion, in the lower, it was enlarged and evidently contained fluid. On section it was found to be distended into a cyst (Plate VI, fig.1); in the lower portion, the cyst wall being formed by the cortical portion of the organ, the cavity by the medullary. In this cavity was a dark coloured granular and grumous fluid, which on microscopic examination, was found to contain granular débris, yellow-coloured /



Fig 1

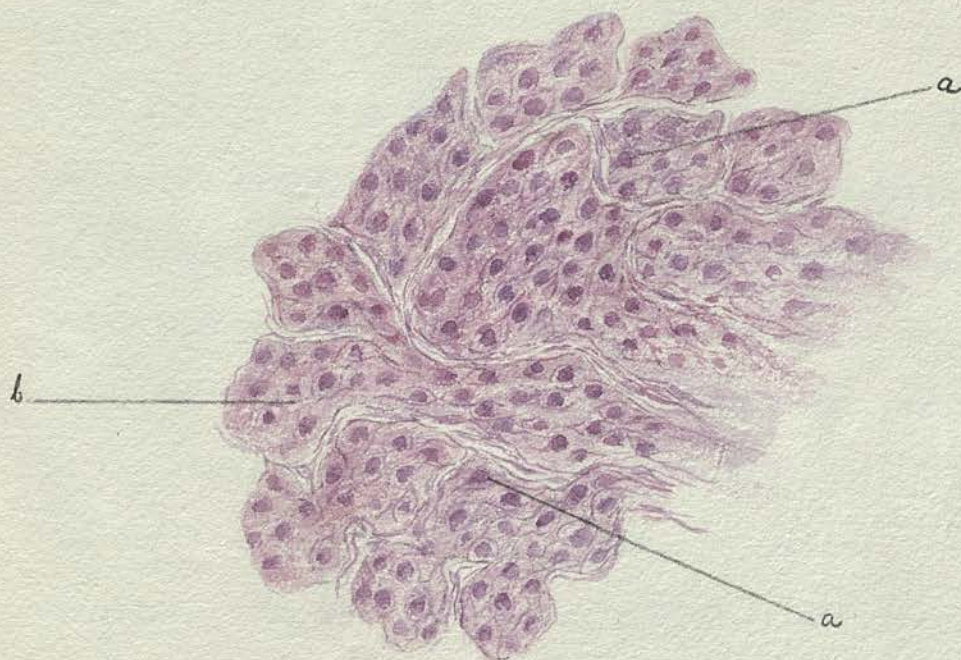


Fig 2

PLATE VII.

Fig.1. - Kidney. x 880.

- (a) convoluted tubules in the epithelial cells
of which are small masses of pigment;
- (b) a small vessel with thickened walls;
- (c) inter tubular tissue increased;

Haematox. and Eosin,
Case XII., see also p.78.

Fig.2. - Liver. x 280.

- (d) portal spaces showing increase of fibrous
tissue (cirrhosis);
- (e) lobule of liver showing large numbers of
red blood corpuscles between the liver
cells.

Case I., see also p.86.

coloured cells and pus-like corpuscles showing fatty degeneration.

The medulla in the upper portion was well-defined, and appeared somewhat firmer than usual.

Pancreas. This was very much firmer than usual.

Kidneys. These were enlarged, firm, and, on section, pale with a broad cortex. There seemed to be considerable increase of interstitial tissue, and towards the apices of the papillae were somewhat glistening pale areas. The capsule stripped easily. Weight of the two organs - 10 ozs.

Intestines. The small intestine seemed somewhat atrophic, and the mucous membrane catarrhal, but no ulceration was found. The agminated follicles appeared slightly more distinct than usual. The large intestine showed considerable thickening of the coats, and general follicular ulceration, with here and there some larger patches of ulceration, some being about $\frac{1}{2}$ inch in diameter.

No distinctly enlarged lymph glands were found, though a few in the mesentery appeared somewhat increased in size, but not more than is usual in catarrhal conditions of the intestine.

Microscopic Examination.

Spleen /

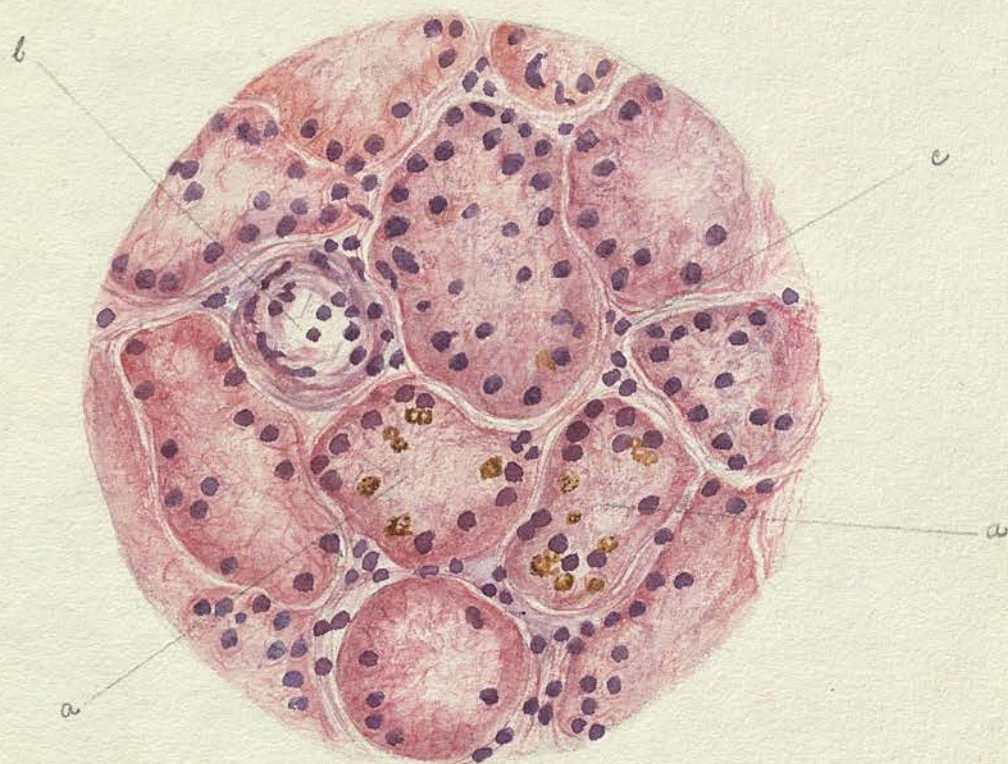


Fig 1



Fig 2

PLATE VIII.

Fig.1. - Spleen. x 240.

showing the deposit of haemic pigment in the spaces between the fibrous tissue of one of the trabeculae. The pigment has been treated with ferrocyanide of potass and weak hydrochloric acid, which has caused it to become blue. The tissue is stained with eosin.

Case I., v. p.172.

Fig.2. - Spleen. x 900.

showing a fibrous area in the organ;
vide p.85.

- (a) large nucleated cells;
- (b) small vessel.

Spleen. The capsule is considerably thickened and from it there are well-marked trabeculae passing in, which are much more fibrous than usual, being in some parts of the section very broad and dense. Scattered through the section are areas engorged with red blood corpuscles and very suggestive of haemorrhages. The Malpighian corpuscles are in many instances unaffected; in others they appear to be undergoing a process of sclerosis, being sometimes reduced to mere knots of fibrous tissue with thickening or occlusion of the arteriole. The whole process is similar to that already described in the last Case. In some parts are areas which are quite fibrous, corresponding to the pale patches seen on naked-eye examination; some of these are apparently trabeculae, the margins of which are encroaching on the neighbouring reticulum by a process of transformation into fibrous tissue; others seem to be independent patches of reticulum in which there is considerable deposition of fibrous tissue. In the spaces between the strands of the former is sometimes a quantity of pigment, (Plate VIII, fig.1.) which takes on a blue colour on being treated with ferrocyanide of potassium and dilute /

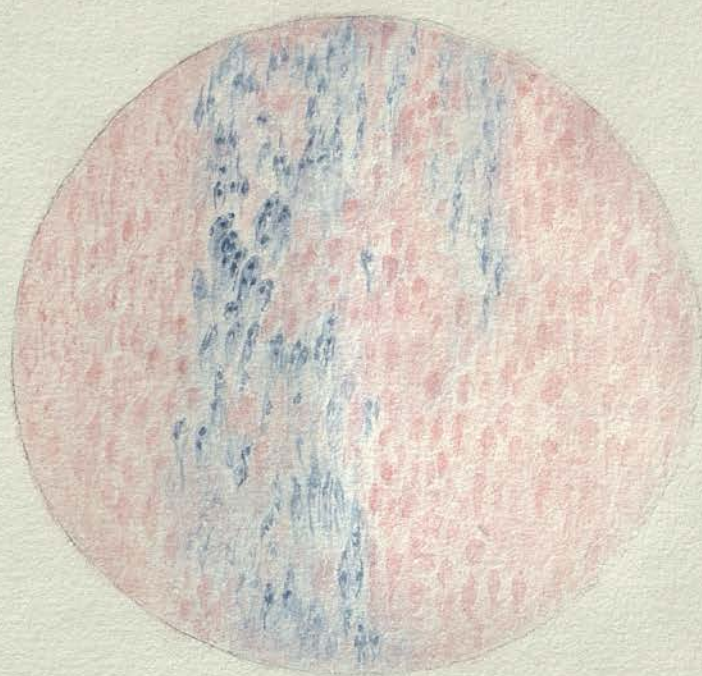


fig 1



fig 2.

dilute hydrochloric acid. The reticulum elsewhere appears very much more dense than normal. On higher magnification, there appear a great number of large cells, lying in the venous spaces of the pulp. These contain several red blood corpuscles, are nucleated and measure 30μ or more in diameter (Plate IX, fig.1). In some places they are found lying in sinuses which contain a large number of red corpuscles, and then they seem to take up a position next the wall of the sinus. They are much more numerous in some parts of the splenic tissue than others, being most plentiful in those portions which are least fibrous.

The pale areas are also found under a higher power to be made up of an irregular fibrous tissue (Plate VIII, fig.2.), and scattered through it are large cells with deeply staining nuclei, while lying in the spaces between the fibres, may be seen columns of red blood corpuscles and at the margins of these patches there is a much greater quantity of blood in the reticulum. Everywhere in the neighbourhood of these fibrous areas are thickened trabeculae, and where the reticulum has become abnormally dense, the number of lymphoid cells is greatly below the usual; and /

and in the vicinity of the sclerotic Malpighian corpuscles, their gradual disappearance may be noticed.

Liver. The lobules are somewhat more distinctly marked out than usual, and there is considerable dilatation of the intralobular capillaries; these latter often containing a large quantity of blood corpuscles. The columns of liver cells lying between them are somewhat atrophied, and show considerable granularity of the protoplasm. Those cells in the central area contain fatty granules, while in the outer two-thirds of the lobule there may be seen distinct pigment granules lying in the liver cells. This, though quite distinct does not occur to the same extent as in the former case. It takes on the same coloration with ferrocyanide of potassium and hydrochloric acid. In the portal spaces there is a distinct increase of connective tissues, especially round the vessels; the bile ducts do not appear affected, (Plate VII, fig.2.)

Pancreas. There is a marked sclerosis of the organ, many of the lobules being invaded by connective tissue from the periphery, becoming eventually quite fibrous, and presenting a dense hyaline appearance.

In /

PLATE IX.

Fig.1. - Spleen. x 1100.

(a a a) Three large cells containing red blood
corpuscles, lying in a venous sinus;

Haematox. and Eosin,
Case I., see also p.85.

Fig.2. - Suprarenal. x 600.

showing groups of gland cells (c) under-
going invasion by fibrous tissue (d);

Taken from Plate VI, fig.1.
Haematox. and Eosin.

In some places, isolated groups of glandular cells may be seen surrounded by connective tissue(Plate X, fig.1.) There is some dilatation of the periacinar lymph spaces.

Suprarenals. The right is cystic, as already described, and under a low power, the cortex, which forms the cyst wall, is found to have the ordinary tubular arrangement of cells, but in the reflected portion, the glandular tissue shows infiltration by new fibrous tissue and round cells (Plate IX, fig.2). This invasion causes the gland tissue in parts to be divided into irregular areas, consisting of small groups of glandular cells. Under a high magnification, these cells are found to be considerably atrophied by the pressure of the encroaching tissue. In the upper leaf of the organ the medullary portion is present, and here also is some early sclerotic invasion, while the arterioles show considerable thickening of their coats. The left suprarenal seems to be wholly converted into a mass of fibrous tissue. On section, it is pale, firm and somewhat glistening, and does not show any appearance of the usual arrangement of the organ. In this dense tissue, several small /

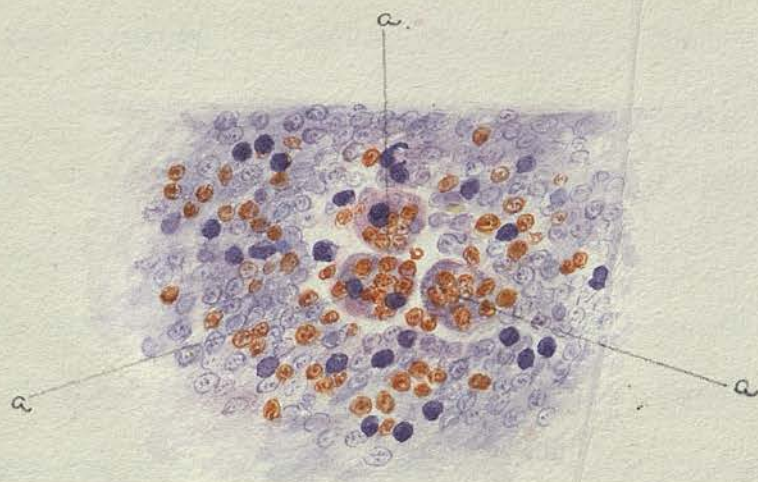


fig 1

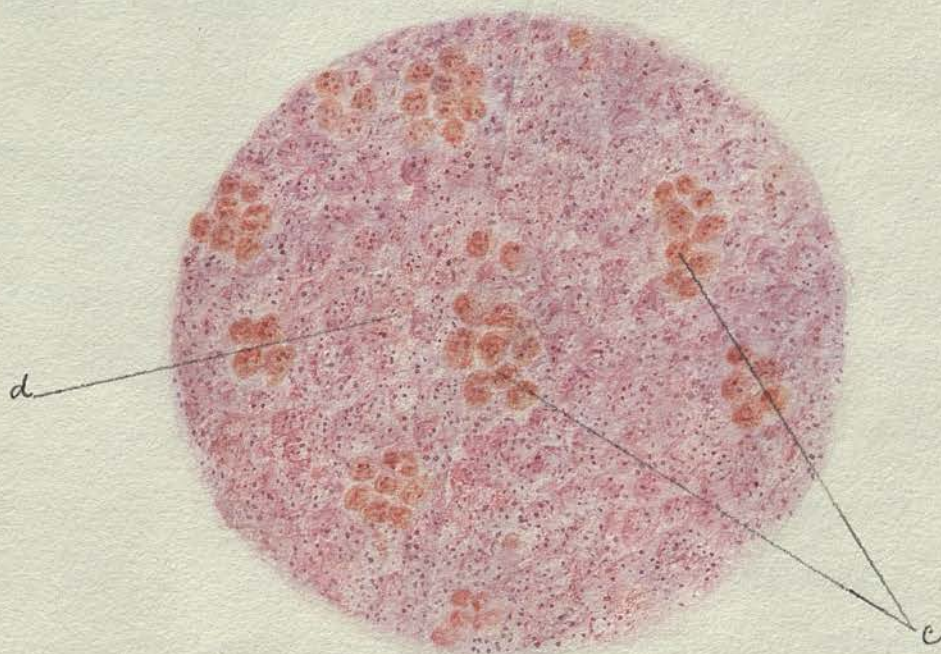


fig 2

small, slightly yellow areas are seen, by a low magnification, consisting of granular cells, arranged in an irregular manner, and surrounded by a dense band of connective tissue, which has an almost hyaline appearance. Under a higher power, these granular cells are apparently atrophic glandular cells, and the connective tissue is very close, containing very few nuclei. Outside this, the fibrous tissue is more open and contains many more nuclei. In this tissue are many small irregular blood vessels (Plate V, fig. 2). In some parts of the organ there is apparently less sclerosis, and consequently a few areas are seen in which there are some more distinctly glandular cells; they are, however, irregularly arranged, do not resemble the normal structure, and show degenerative changes. Scattered through these areas are small fatty granules. There is some increase of the fibrous tissue round the whole organ, and in this are found vessels, showing some thickening of their coats.

The Intestines. The small ^{intestine} shows considerable catarrhal change of the mucous membrane; the vessels in the submucous coat are engorged, and the capillaries show some thickening of their walls. There is apparently no change in the villi beyond the catarrh /

catarrh. There does not appear to be any deposit of lymphoid tissue, nor can any abnormality be discovered in the nerve plexuses.

In the large intestine, there is also considerable catarrhal change and thickening of the mucous and submucous coat; even the muscular coats, appear thicker than normal. Between the Lieberkuhnian follicles there is some increase of fibrous tissue. No lymphoid growth is to be seen.

The Kidneys. On microscopic examination these present marked interstitial changes, there being a considerable increase of connective tissue between the tubules, and great thickening of the capsules of Bowman. This new tissue appears to have exerted a certain amount of pressure on all the tubules, causing a diminution in their lumen; in these tubules the epithelium appears cubical, granular and degenerated. In some of the tubules distinct granules, taking on a blue colour, are seen on treating the sections as already described; these lie in the cells of the convoluted tubules. The vessels also partake in the general thickening, especially the capillaries, these being apparently the part of the organ most affected.

From. /

From this account of the morbid anatomy, the descriptions of other writers differ considerably in many important points. The only author who gives any full consideration to the subject is Banti (12); Bruhl (13) and Labadie-Lagrave (15), merely reproduce his work; the former admitting that he has made no personal investigations. The first point to which I would draw attention, is the condition of the kidneys, which, as I have shown, present considerable changes. It will be remembered that, when considering the urine, it was stated that albuminuria was much more common than appears from the accounts given by the writers already mentioned. The first account given above is from a patient dying at 40, the second at 39, both females: thus the marked interstitial and other changes can hardly be the result of any primary and independent kidney condition.

In many cases it does not appear if a microscopic examination were made of the kidneys, and it would almost seem as if such were not the case from the way in which the organs are described. It may well be, therefore, that the important lesion present in the kidneys in other cases, may have been missed in others.

Williamson /

Williamson (17) does not give any histological description of these organs. Banti says distinctly that the kidneys do not show any of the changes found in nephritic conditions; the statement therefore, requires considerable modification. Certainly none of these authors mention the occurrence of pigment in the cells of the convoluted tubules, the only mention of any such appearance is by Dr Saundby (19) in the account of Case XVI., which was evidently one of splenic anaemia, although the diagnosis was left open. In one remarkable way, Case I., (the second of the two given above), differs from any other account of the morbid anatomy of this disease - in the curious condition of the suprarenals. In no other instance, is any full report given as to the state of these organs. Banti (12) dismisses them as appearing healthy, seemingly, without microscopic examination; while other writers make no mention of them as a rule. Unfortunately in Case XII, the first of those I examined, the suprarenals were omitted. That the condition of these organs may have a very important bearing on the case, I believe to be probable. It will be seen from the macro- and microscopical examination in Case /

Case I., that they had undergone considerable morbid change. Also in Cases 2, 3, 4, 6, it will be remembered there was distinct pigmentation, occurring in patches in Cases 3 and 4, but more diffusely in the axillae, etc., in Cases 2 and 6. As no opportunity has yet arisen for verifying the supposition that the suprarenals are diseased in these cases, it can only be a matter of surmise that they are so. At the same time, additional evidence is found in the asthenic condition of the patients. This will, however, be more fully discussed when considering the pathology. It will be important in this connection to refer to the two Cases, Nos. XV. and XVI, quoted from the account given by Dr Saundby (19) of Birmingham, under whose observation the cases came. In Case XVI, the autopsy showed the following conditions.

Abdomen. The spleen occupied the whole of the left hypochondrium, wt = 66 ozs. It was dark purple in colour, hard and tense. On section it looked like damson cheese. It gave no amyloid reaction. Under the microscope a large quantity of granular brown pigment was diffused through the pulp. The liver appeared normal. The stomach was dilated and catarrhal.

The /

The kidneys were rather large, their cortices looked dark, and the medullary portions pale. Under the microscope, pigment could be seen lying in the tubules. The suprarenals were very small and atrophic; $R^t = 18$ grains, $L^t = 10$ grains. The semilunar ganglia appeared normal. Microscopically the suprarenal showed extreme atrophy, but no other apparent change. The semilunar ganglia showed no microscopic change. I have been enabled to examine the preparations of these organs, and find that the above account is correct. It would seem, therefore, from these facts that in some of these cases, there may be important changes in the suprarenal capsules, changes whose significance may be great, and which perhaps have important bearings on the pathology of the disease. Unfortunately observations on this point are far too few to warrant any conclusion being drawn, though at the same time, the fact, that the organs showed morbid changes in two of these, at the best, unusual cases while other cases show abnormal pigmentation, is one which deserves careful consideration.

The Pancreas is stated by Banti (12) and Williamson (17) to be normal; other writers do not seem /

seem to have made any special investigation. From the description given above, it appears that the organ may undergo a process of cirrhosis, and to a very considerable extent. Whether this is coincidental or not is uncertain, but its occurrence in two cases is worthy of consideration.

The Liver. Here we also find considerable differences in descriptions. It seems as if a certain increase of interstitial tissue is usual; Banti (12) speaks definitely of a multilobular cirrhosis and Williamson (17) in his case also found increase of the connective tissue in the portal spaces. In Case I., I found decided deposit of fibrous tissue in this part of the organ as described, but in the other it was extremely doubtful if any increase had taken place. It seems as if the liver underwent increase in size in the majority of cases. This may vary however, so that at the autopsy a liver of average size may be found. The liver cells are probably always more or less altered, the general condition being atrophy and fatty degeneration, the intra-lobular capillaries being dilated. The amount of fat in the liver cells may be very marked sometimes. The most interesting point /

point is the presence of pigment. This has not been noticed by any previous writer except Strümpell (23), who, does not give any details as to its situation, or origin. The presence of pigment here is a most important factor in the pathology of the disease; it is, however, variable in quantity and, it may be, that this depends in some manner on the acuteness of the case as will be shown in discussing its causation later on. The biliary vessels do not show any alteration. The chief interest, of course, centres round the spleen, and there are considerable differences in some of the descriptions, due no doubt to the fact that the spleen itself shows very considerable variation. In the description of the post-mortem appearances in Cases XII, and I., this is brought out, for in the first the spleen presented a uniform dull red surface on section, while the other showed some more fibrous areas. These are the two main differences in records of autopsies, some describing the spleen, except for its size and consistency, as presenting no naked-eye abnormality, while others mention these fibrous patches. Microscopically there are corresponding differences. Thus, in some cases distinct pigment granules may be seen lying in the spaces between the /

the strands of trabecular tissue; in other cases the amount of pigment is small; the splenic reticulum may be generally thickened, or there may be more fibrous tissue in some parts than in others. The presence of large cells containing red blood corpuscles is a condition mentioned, so far as I can find, only by Williamson and in this paper. This is a point of the utmost importance, for it is, I think, definite evidence of haemolytic changes taking place in the spleen, and is, moreover, an interesting fact in splenic physiology and pathology. As to the origin of these cells, they seem to be endothelial cells coming off from the venous sinuses or spaces in the reticulum, and which then take into themselves the red corpuscles which then break up, the blood pigment being either deposited in the spleen tissue, or carried to the liver. Why this difference occurs we shall see presently.

Bone Marrow. This structure has been examined by Banti (12), Strumpell (23), and Williamson (17). Unfortunately, in both cases where I made an autopsy, permission could only be obtained for the abdomen, so I was unable to investigate the bone marrow. Through the /

the kindness of Dr.R.T.Williamson of Manchester, I have been able to have microscopic preparations of the marrow from his case (No.XIII). The naked-eye characters, as given by the writers just mentioned, show that there is conversion of the yellow into red marrow in the long bones. Banti (12) (p.68) describes it as of a clear, red colour and gelatinous.

Williamson's account is more complete. He found the marrow of the sternum and from the middle of the shaft of the humerus "dark purple red" in colour. This description shows that profound changes have taken place in the bone marrow, these being apparently most marked at the middle of the long bones, and showing a complete disappearance of the fatty form, with probably absorption of the bone spicules.

From microscopic examination I made out the following conditions, after staining with haematoxylin and eosin. There is complete absence of fat cells. Nucleated red blood corpuscles appear in considerable numbers, but colourless cells though present are not seen in any quantity (vide, Plate X, fig.2). There are also many ordinary red blood corpuscles to be seen. Eosinophilous cells are rarely to be seen.

There /

PLATE X.

Fig.1. - Pancreas. x 280.

- (a) group of acini becoming surrounded and
invaded by fibrous tissue (d)

Haematox. and Eosin,
Case I., vide p.86.

Fig.2. - Bone Marrow. x 1100.

- (c) large nucleated red corpuscles;
(gigantoblasts)
- (g) ordinary nucleated red corpuscles;
- (r) nucleated red corpuscles showing a rosette
nucleus;
- (h) ordinary red corpuscles;
- (b) colourless marrow cell;
- (p) small mass of pigment;

Case XIII., v.p.226

There are in considerable numbers, large red cells measuring at least 30μ in diameter, showing a large irregular nucleus, and besides these, others equally large are seen to contain ordinary red blood corpuscles. Examined more in detail, the nucleated red corpuscles show much variation in size; the nucleus is, in some cases, rosette-shape, in others, appears to be undergoing fragmentation. Some even show two nuclei.

The large nucleated red cells (gigantoblasts) form a particularly striking feature (vide figure 2), and also show some variation in size. Indeed, all sizes may be found from the ordinary nucleated red corpuscles up to these cells measuring many times the diameter of the former. Small masses of pigment may be seen, in some instances, free between the cells, in others, apparently enclosed in other cells.

The Alimentary Tract.

Changes in the intestines have been noticed in some cases, the chief being ulceration at various parts, and, in some instances, some swelling of the Peyer's patches and solitary follicles with general catarrh of the mucous membrane. Death from peritonitis has resulted on more than one occasion, being recorded by Müller /

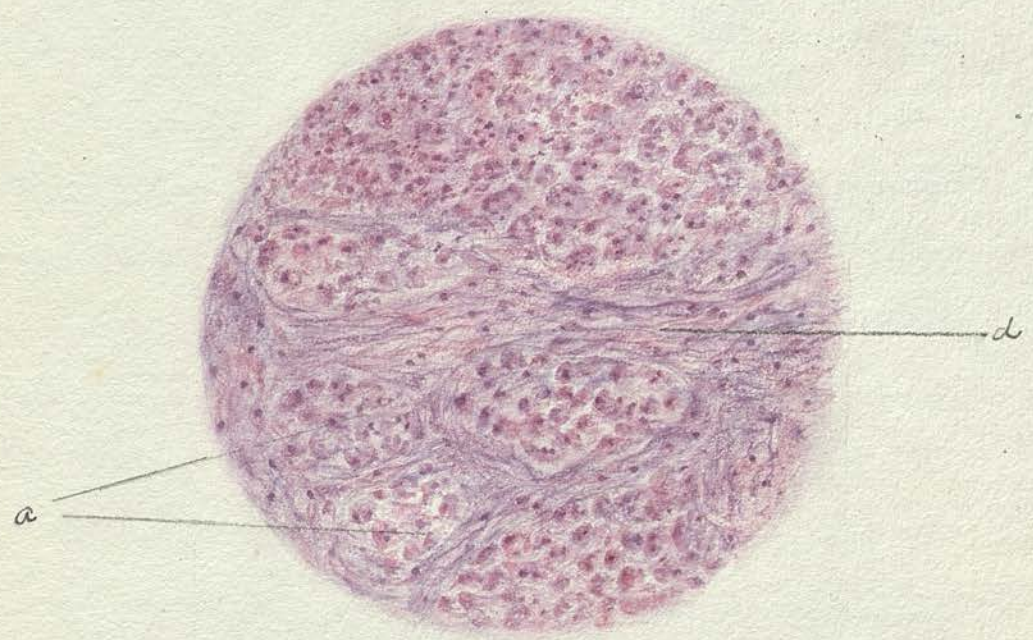


Fig 1

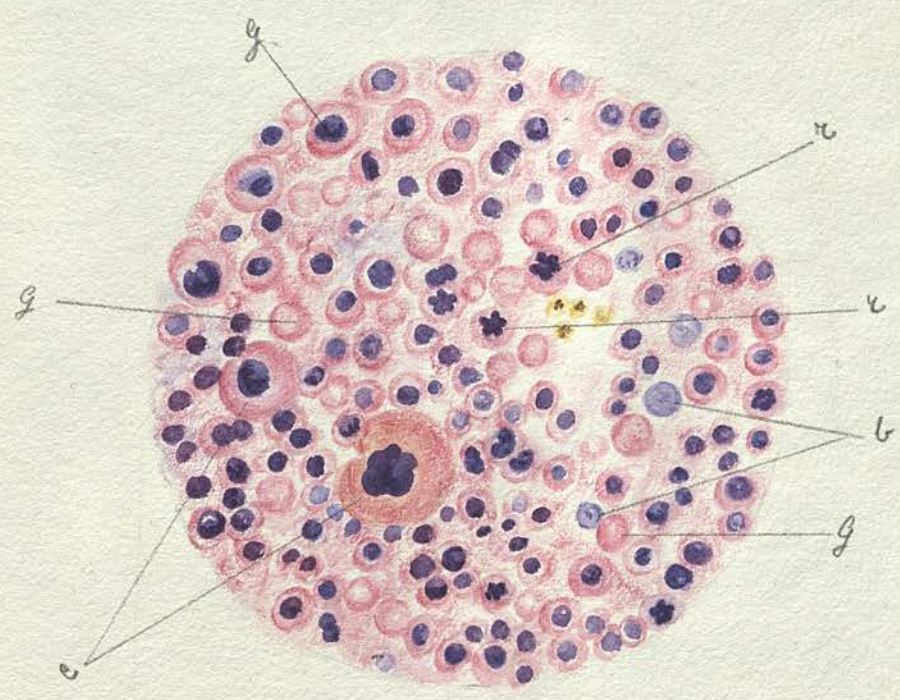


Fig 2

Müller (3), and Williamson (17), in both of which cases, a perforated ulcer was found in the small intestine, in the jejunum in Müller's, in the ileum in Williamson's. In the latter, several other ulcers were found in the lower part of the ileum, running transversely to the long diameter of the gut, but there was nothing to suggest any of the usual forms of ulceration. In my own case, No. I., there was no ulceration found in the small intestine; the mucous membrane, however, being very catarrhal and the solitary and agminated follicles were more distinct than normal, being in fact in the condition usually found when certain changes are taking place in the mucous membrane. In the large intestine there was marked thickening of the mucous membrane, and a considerable amount of follicular ulceration with here and there much larger patches. The mucous membrane microscopically, appeared very catarrhal, and there seemed to be some general thickening of the sub-mucus coat with some fibrosis between the Lieberkuhnian follicles.

The Thoracic Organs.

The lungs may show a certain amount of hypostatic pneumonia, and at the base of the left, there may be considerable /

considerable pleuritic adhesion. There are no special features to note otherwise.

The heart shows the conditions common to all anaemias, being dilated, flabby, and its muscle in a state of fatty degeneration. The endocardium may, however, show evidence of inflammation, for in some cases, considerable thickening of the valves has been found, and in William-son's case there was marked endocarditis. In my own Cases II and III, there were, as will be seen in the clinical account, marked murmurs other than haemic. In Case III, the valve change was probably due to previous acute rheumatism, but in the other there was nothing in the history indicating such a condition.

The thyroid has not shown any changes in any of the Cases, except in Case VI, where there was a fairly marked goitre, the patient showing also exophthalmos. There are very few details as to the nervous system. I have examined the semilunar ganglia from one case, No. XVI, and was unable to detect any abnormality. Banti⁽¹²⁾ however, says he observed 'lymphoid infiltration'(?).

This completes the description of the pathological anatomy, and from it we see that marked and important changes are present, which are very characteristic of the disease. It remains now to consider the pathogenesis of these changes.

Having /

Having now considered the clinical course and post-mortem appearances, we are in a position to study the pathology of the disease. That this is extremely obscure, there is no doubt, and nothing could indicate this fact so strongly as the variety of names which different authors have used in describing cases. These various names have already been referred to¹ in the opening chapter, but it will be necessary to recall them in comparing the various theories which have been advanced as to the nature of the disease. From what has been said as to symptoms, it is evident that we have to do with a disease attended by profound anaemia. All authors are agreed on this point, but then comes the question whether this anaemia is a primary or secondary condition or, in other words, is the blood state merely symptomatic of some lesion, or is it the result of changes in the haemic system itself? We know that in certain wasting diseases, there may be a marked anaemia in which the blood changes may be very important. Such conditions as malignant disease and several /

several morbid states of the stomach and intestinal tract may all cause severe anaemia. In all these, however, the blood changes are not the main symptoms, or most prominent feature in the pathological anatomy of the case; they are obviously secondary to some other condition, whereas in certain other diseases, the morbid characters of the blood are much more prominent than any other lesion, and may therefore be considered primary. Of course all anaemias may be looked upon as secondary in a sense, to some other condition, but this is an essential part of the pathology of the anaemia in question, for the organs primarily at fault are in direct relation, being part of the haemic system whether constructive or destructive. In these forms therefore, we have what we may call a primary anaemia as distinguished from a secondary or symptomatic form.

To which of these classes does the disease we are considering belong? There cannot be much difficulty when we consider its clinical features and the absence /

absence of any more prominent anaemia-producing disease, in concluding that, whatever its pathology, the disease is one chiefly of the haemic system. At the same time, this question simple as it may appear at first sight, involves one or two points which may perhaps be approached with more advantage later when the relations they bear are being worked out; it then will be easier to show their connections.

^

The majority of those writers who have described cases seem to have considered the disease as one of the haemic system, but beyond this, they differ extremely. It will be advisable therefore to review the various theories put forward.

The earlier writers, such as Griesinger who noticed the existence of cases like these, seem to have taken them for a form of leucocythaemia and Woillez (1) speaks of his case as hypertrophy of the spleen with symptoms of leucocythaemia, without exaggeration of the number of white corpuscles in the blood. From the account of the blood given above, as also the details of the post-mortem appearances, there is not much difficulty in coming to a definite /

definite conclusion that these are not cases of leucocythaemia. But is it possible that they may be anomalous forms of that disease? There does not appear in view of recent work on the nature of leucocythaemia to be anything to support this hypothesis; Splenic enlargement does not constitute leucocythaemia, nor does it indicate any generic relation with that disease, for as shown by Müller and Rieder (32) Muir (33) and myself (25) the essential character of leucocythaemia is the presence in the blood of abnormal forms of white corpuscles, as well as actual increase, of some, (at any rate) of the ordinary white-cells. If then there be no increase of white corpuscles, to say nothing of the absence of anomalous white cells from the blood, it is impossible to conceive of these cases being leukaemic in nature, or even having any relation to such a condition.

Strümpell as already mentioned, in using the term 'Primitive Splenic Anaemia' seems to have given rise to the idea that this disease is a primary affection /

affection of the spleen, and this way of looking upon it has practically lasted up to the present day, for in the recently published work of Labadie-Lagrave ⁽¹⁵⁾ this is the title of his article, and as an unimportant variation, is the term 'Splénomégalie Primitive' used by Brühl ⁽¹³⁾, and which also indicates the position he takes up regarding the pathology of the disease.

Strümpell ⁽²³⁾ found the spleen, post-mortem, to show merely venous dilatation, and on the strength of this he bases his idea that 'Splenic Anaemia' may be the result of chronic hyperaemia of the spleen; that is to say, the chronic congestion would seem to start certain changes in the organ which result in the production of the various symptoms.

In support of this, there is extremely little. Chronic hyperaemia of the spleen is a common occurrence, and were the clinical conditions, described above, the result, such a disease would be an extremely common one, instead of the rare one which all admit it to be. Moreover, in the various autopsies, no adequate cause for back pressure on the spleen /

spleen, to more than a slight degree has been found. It is true that in some few cases, mitral lesions have existed, in others a slight amount of hepatic cirrhosis, but it is evident from a consideration of all the circumstances in these same cases, that the amount of back pressure was quite inadequate to cause the definite changes in the spleen, or to originate the very distinct clinical characters.

Banti[§] indeed criticises Strümpell's case in the severest possible manner by refusing to consider it as one of 'Splenic Anaemia' on the grounds of its intermittence, and the beneficial effect of treatment; he states that in his opinion it was an instance of pernicious anaemia, the splenic enlargement being secondary to the oligocythaemia. Here, however, Banti was in error, as a review of the description of the clinical course as given already, will show.

Müller, who also maintains the primary splenic character /

§ op. cit. p. 59.

character of the disease, would explain the condition by assuming that the splenic tumour would be produced by the retention in the spleen of a large excess of lymphoid cells, which for some reason or other, cannot escape into the blood current. This is taking for granted however, that such elements are formed in excess, which is certainly not a fact supported by a study of the morbid anatomy of the spleen. Nor would this theory, supposing it to be the correct explanation, account for the general symptoms. We must have difficulty in accounting for the invariable absence of leucocytosis, for it would seem impossible to imagine a large production of lymphoid cells in the spleen without their appearance sometime or other, especially during the periods of remission, in the blood. We may consider therefore that this theory of Müller's is untenable.

Reference has already been made (p. 2) to the proposition put forward by Gowers in explanation of splenic anaemia, that it consists in a retention in the spleen of white blood corpuscles. The spleen condition /

condition is here looked upon as one of hypertrophy. From consideration, however, of the microscopic characters of the organ, it may more justly be concluded, that we have not to do with such a lesion, and that in reality, the lymphoid elements in the spleen are, on the contrary, greatly reduced. In a sense we may look upon the enlargement of the spleen as hypertrophic, but not from the point of view of this being the cause of the disease.

If we turn now to Banti's theory, that the disease is a primary splenic lesion, or as he terms it, a 'primitive splenopathia', we meet with a more difficult question, especially when it is added that he looks upon this condition as a purely splenic form of lymphadenoma.

In support of the primary splenic lesion, he adduces the following points, (a) that the first symptoms complained of by the patient are weight and pain and a dragging sensation in the left hypochondriac region; (b) that the patients do not complain of anaemia till sometime after the onset of these symptoms; /

symptoms; (c) that the first thing noticed is the splenic tumour; (d) and, above all others in importance, the fact that there is a considerable want of relationship between the symptoms and the size of the splenic tumour; that is to say that the latter may have reached a considerable degree before the anaemia becomes a striking feature. These facts, he says, would remain incomprehensible were the splenic tumour a secondary phenomenon. Lastly, as convincing evidence he says that patients who have had the spleen removed have recovered from the disease. It may not be inadvisable to quote Banti's own words; he says (p.100) "these two facts - (1) the precedence of the splenic hypertrophy to the other signs of anaemia; (2) the recovery of the patient after extirpation of the hypertrophic spleen, seem to me to demonstrate the evidence of the splenopathia not being a secondary condition, but that there may be an anaemia dependent on the idiopathic hypertrophy of the spleen, and consequently it is impossible to deny the existence of the distinct nosological type - splenic /

splenic anaemia."

Brühl also holds that, "the affection would be the consequence of an alteration of the spleen, the other haemopoiëtic organs only taking a small share, in the morbid process; the clinical picture described would be therefore the symptomatic expression of the splenic lesion".

As these authors take up such a definite position, it will be necessary to examine the grounds on which they base their conclusions. Banti's first argument that the splenic hypertrophy precedes the general symptoms is not the invariable rule, and had he been able to examine a larger number of cases, there can be little doubt he would have avoided this fallacy, and indeed, in his chapter on the symptomatology, he does not seem so sure of the fact, stating that it would be of great practical and scientific interest to know if the splenic hypertrophy precedes the other signs of the disease. From a study of several cases, there seems to be little doubt that in /

in many instances, there is a longer or shorter history of weakness, pallor, etc., before anything pointing to the presence of an abdominal tumour was noticed. Here the study of hereditary cases is especially important, for in some of these cases, the various symptoms of anaemia have been noticed, and then the gradual development of a splenic tumour.

From a careful study of these cases, it seems quite possible to have a blood value much below the normal without any great evidence of constitutional derangement. In the absence of blood estimations, in any case, it would be unsafe to say that there was no anaemia until after the splenic tumour appeared. Consequently in several cases, we have actual evidence that there were signs of anaemia previous to the existence of splenic hypertrophy, while in support of the opposite theory that this latter was the first thing, the anaemia being secondary to it, is founded only on the most uncertain evidence. In several cases, there is the clearest possible evidence that the patient was unconscious of anything of /

of the nature of an abdominal swelling when the history of weakness, pallor, etc., had already been of considerable standing. If, therefore, the earliest symptoms had been, as Banti would have us believe, pain, weight and dragging in the left hypochondriac region, it is more than probable that an enlarged spleen would be perceived by the patient and friends early on in the history of the case, instead of their complaining for long periods of weakness, etc.

Banti finds in the want of relationship between the size of the spleen and the severity of the symptoms important support of his theory. It is difficult to see how this can be. As already shown Banti either does not acknowledge or does not recognise that there may be intermittence of all the signs and symptoms of the disease, including the splenic enlargement. If, therefore, any idea as to the progress of the case or the severity of the lesions be founded on the size of the spleen, it must necessarily be fallacious, and a large spleen without severe anaemia is not unusual, when the disease has lasted for /

for a considerable period. Indeed, if any conclusion can be drawn, it would rather point to the splenic condition being secondary than primary.

The next point of importance raised by this author is that those patients who have survived splenectomy, recover from all the symptoms of the disease; this is not based on sufficient evidence. He gives a table (op.cit. pp 116-117) of the results of the splenectomy for various conditions, and of 21 cases quoted, the diagnosis of splenic anaemia is given in four only; of these one did not recover; of the other three (recoveries) one had leucocytosis and may perhaps have been a case of leucocythaemia, so that only two remain in which the diagnosis may have been correct. Two cases do not warrant the conclusion that the writer draws.

It is not to be supposed from what has been said that the splenic tumour always follows symptoms of anaemia. This would not be correct, for the history of some cases certainly shows that an enlarged spleen is sometimes discovered accidentally, the patient not complaining /

complaining of any special ill-health; but then, there is probably always a blood value below the average, and there is no guide as to how long this may have lasted, or what relation it bore to the spleen. It is evident when we compare these theories with the clinical history, that none of them is adequate to account for all the symptoms, and at the same time to correspond with the morbid anatomy; thus in those cases which have been most fully described, many points are passed over, or mentioned in a cursory manner which recent investigations into the pathology of anemia have shown to be of prime importance.

From a study of the cases, which are here and elsewhere recorded, I suggest the following theory in elucidation of Splenic Anaemia :

The disease called Splenic Anaemia consists in a Pathological Haemolysis, progressing by repeated attacks of blood destruction, and characterised by intermittence in the process, when there may be amelioration of the symptoms; accompanied by definite changes in certain organs, and ending fatally after a course, variable in length.

In /

In support of this proposition we must study in detail :-

- (1) The symptomatology, as pointing to a destructive anaemia with periods of quiescence.
- (2) The morbid anatomy in evidence of this.
- (3) The probable pathogenesis of this anaemia.

(1) From the account of the mode of origin, we learn that there is a condition of anaemia, with loss of strength, and all other signs of such a state from a very early period, and that although, such appearances may be only temporary, still they are repeated till the patient develops a much more obvious facies, with various changes, in the colour of the skin, all proving a profound constitutional derangement.

Other phenomena, of frequent occurrence in all anaemic states may be marked features, such as various haemorrhages, as already described. Mention has also been made of purpuric eruption, and reference to Case III (vide p188, also Plate I.,) will show that this may be very marked. This is always an indication, when occurring in the course of anaemia disease of a considerable degree of blood change. We have also /

also seen (p. 23) that there may be conservation, for sometime at any rate, of the sub-cutaneous fat, a circumstance which as is well known, may take place in pernicious anaemia and others.

In a more advanced stage we have all these symptoms becoming aggravated, while the effects on other organs, usual in defective blood states, such as cardiac dilatation, fainting fits, buzzing in the ears, etc., may all be observed. Into these we need not enter more fully, for they only need mention here as showing that we have proof of a marked and progressive condition of anaemia.

If we now turn to the state of the blood as already described (pp 42-56) we find important proof of anaemia. It was there demonstrated that the principal change is an oligocythaemia, which varies within certain limits, but, notwithstanding periods of improvement, tends to become more marked, till finally, the number of red corpuscles may be enormously decreased. Here we must observe that, although profound, this reduction in number of the red corpuscles does /

does not, not, so far as I have ever found, show the extreme degree it does in pernicious anaemia. The fact, as shown in the account of the blood, that oligocythaemia may be noticed in the very earliest stages, even in cases where anaemia would not have been suspected had not attention been directed to them from other causes, is of importance. It shows, I think, clearly that there is from the first some morbid influence at work in the blood.

A point of importance to note is that this oligocythaemia is in no way related to haemorrhages. Of course when such do occur (vide Case XXI.) there is a further diminution of the number of red cells, but in other cases where haemorrhages have not occurred, or have only been noticed at a former period, the amount of oligocythaemia may still be very great. In fact, in some of the cases where the reduction in number of the red cells has been greatest, there have been no haemorrhages. As there is, therefore, no correspondence between the degree of oligocythaemia and haemorrhage, we must look upon the former as the /

the result of some process distinct from mere loss of blood, a condition similar to that found in pernicious anaemia.

We have also seen that variation in size and shape or poikilocytosis is more or less a constant feature, especially the presence of small sized corpuscles. Abnormal shapes are not so often observed. This points merely to the fact that the anaemia is a severe one, for as recent observations (34) on this subject go to show, it may be seen in any advanced anaemia, even in secondary forms, and is not by any means indicative of pernicious anaemia.

The presence in the blood of nucleated red corpuscles (p .52.) is too rare in this disease to warrant any special deductions, but from a study of their probable mode of origin in other cases (33 & 25) it would seem to indicate an attempt at compensation on the part of the bone marrow.

Much more important is the not infrequent presence of the so called Eichorst's corpuscles (vide p 53) ⁵⁻³ X
As shown in the description of the blood it was possible /

possible to watch their formation in some cases. Their mode of origin has been debated, some being inclined to regard them as immature red corpuscles, others considering them to be indicative of an abnormal haemolysis, and as the disease in which they most frequently occur is pernicious anaemia, there is much to be said in favour of the latter being their true significance. They have also been observed in cases where blood destruction has been artificially produced by the injection of certain haemolytic agents as pyrogalllic acid and toluylendi-amin (34).

Their presence therefore in this disease is a point of great interest, for if evidence of blood destruction, they support the theory that such is the pathological process underlying splenic anaemia. On the other hand, there is independently of these cells, and as we shall shortly see, very strong evidence of abnormal haemolysis, and therefore we have corroboration of their being a product of this process, the more so, as in those cases in which I found them, there /

there was a profound and advancing anaemia.

It is very difficult to offer any explanation of the fact that in the early stages, there is a higher relative percentage of haemoglobin than of red blood cells, while later on, there may be an extreme reduction in the amount of both, (vide Cases I. and III.) Is it possible that, in the early history of the case, the loss caused by pathological haemolysis is compensated by an increased production on the part of the bone marrow, and especially by a production of cells rich in haemoglobin, as may be supposed from the fact that red marrow ^{is found} in abundance; and ^A that in this we have the presence of nucleated red blood corpuscles in large numbers. In other conditions of anaemia, the substitution of red for fatty marrow is also seen, and it is probable that the change is in a manner compensatory, and is able for a time to supply haemoglobin holding cells. Afterwards there is probably a failure in the supply from a gradual progression in the pathological conditions, and thus we find the quantity of haemoglobin falling.

It /

It will be remembered that in Case IV, there was a marked improvement in the quantity of haemoglobin (vide p. 54.), this increase being quite out of proportion to that of the red corpuscles. This is in favour I think, of the idea that the bone marrow is in a condition of increased activity, and therefore, of the conclusion that we have not to do with a defective haemogenesis.

Passing now to the consideration of the urine and its constituents as given in a previous chapter, we are at once met by a most important piece of evidence in support of the haemolytic theory, viz., the presence in the urine of pathological urobilin. This may be at times very marked, giving the urine a very characteristic colour already described, or in some cases, it may be a more or less constant feature. When we find that this pigment appears in great quantity during an attack which is otherwise characterised by an increase in the anaemia, it is plain that it has an important significance as an indication of certain changes taking place in connection with the haemic /

haemic system. It would be impossible within the limits of this paper, nor indeed is it necessary, to give the various details, so far as research has gone, as to the presence of certain pigments in the urine. We must however, refer to some of the facts briefly. As shown by MacMunn, pathological urobilin appears in the urine as a result of certain blood states such as haemorrhage, and also in conditions of blood destruction independently of extravasations. This pigment - pathological urobilin - is quite distinct from the 'Normal Urobilin' of urine, and is not found, even in cases of anaemia, due to ordinary causes. This latter is probably derived from haematin, most likely by the action of nascent oxygen. Pathological urobilin is, however, a product, probably of bile pigments, and as we know, these are largely increased by a greater supply of haemoglobin to the liver, as by haemolysis. Now, as stated above, the faecal matters always remained 'high coloured' being even in some cases, more so than usual, especially /

especially during attacks. We also know ⁽³⁵⁾ that there is a close similarity between pathological urobilin and stercobilin and that there is even a closer resemblance between stercobilin and urohaematoporphyrin; at the same time certain bands are missing from solutions of the two former compared with similar solutions of urohaematoporphyrin, "suggesting that the two former are more complete metabolites of haematin than the latter", (MacMunn op. cit.) From this we learn, first, that haematin is being conveyed to the liver in abnormal amount, more so in fact than the liver is able to deal with, and consequently, pathological urobilin appears in the urine. When however, the normal process is still more deranged we may find urohaematoporphyrin in the urine, as was the case in some instances. This would also point to a possible double origin for pathological urobilin, because urohaematoporphyrin does not appear to have a biliary origin; consequently we must suppose that a destruction of haematin is taking place in other situations as well as in the liver.

Besides /

Besides the evidence as to haemolysis of pathological urobilin in the urine, a condition which is common to splenic anaemia, pernicious anaemia, and some other conditions, we may have other evidence in the occurrence of methaemoglobin. This is not a feature of pernicious anaemia and rarely of splenic anaemia. It may, however, be present in unusually severe cases, especially, I believe in their earlier stages. In some of the cases (Nos. IV. and XV.), it was found when the patients were suffering from a very acute exacerbation. However it was an unusual phenomenon, even when there was considerable pathological urobilin present. We shall see later why this should be.

Another extremely interesting fact I observed in some of these cases, and which has also been described in connection with other diseases of haemolytic nature (28) (p.328), was the presence of pigment containing cells in the urine. These cells were apparently of renal origin, and were only seen at the time of an attack. As already described, pigment was found in certain situations in the kidney, and doubtless the appearance of pigment-bearing cells was connected with this. Further observations on this point /

point will be made when the pathological anatomy is under consideration, but what concerns us just now is that the presence of such pigmented cells is most likely evidence of extensive haemolysis, extensive alike in its amount and its possible seat.

From the consideration of these clinical facts, we may justly infer that the condition is one of marked anaemia, characterized by exacerbations, with improvement, in the early stages, at any rate, in the periods between them, the whole process being probably one of pathological haemolysis. We may therefore turn to the pathological anatomy to look for additional evidence.

- (2) The morbid anatomy in evidence of this proposition (p. 70-116, et seq.)

The most obvious feature of the spleen as described above, is its size, which it will be remembered, varies during life. It has also been shown that this variation is closely connected with the exacerbations of the disease; consequently we must trace some relationship between the size of the spleen and the abnormal processes going on at the time. Recent researches on the subject of blood destruction (31) go to show that the spleen plays an important role in this /

this process, and that certain traces of haemolysis may be found in the organ, while in cases where the spleen has been extirpated in animals, and then haemolysis induced by the injection of certain blood destructive agents, their effect on the blood is greatly reduced or may even be nil. When the spleen is examined microscopically under conditions of artificial haemolysis, we find that deposits of pigment have taken place in it, and also as shown by Hunter (op. cit.) great quantities of pigment may be found in this organ after transfusion. That this is a special process, and not a mere mechanical collection of pigment, or, to use an expressive term, not a scavenging action on the part of the spleen, there can hardly be doubt; and, as going to prove this, the same author found that "the cells of the spleen have the power of arresting red blood corpuscles before the latter have undergone sufficient changes to allow of their enclosure by leucocytes."

When describing the morbid anatomy of the spleen, it was shown that red blood cells may be seen enclosed in large cells in the meshes of the spleen (p.85.) and also that many local collections of red cells were found /

found, evidently undergoing some modification, while in some parts of the tissue were considerable quantities of pigment, shown to be of haemic origin by its micro-chemical reactions. Now these facts are strongly confirmatory of the theory that the spleen is concerned in haemolysis, or in other words, certain changes take place in the blood which render it physiologically imperfect, and consequently, in its passage through the spleen, it is subjected to certain influences on the part of that organ which are for the purpose of removing the effete blood, the red corpuscles being taken up by special cells, or otherwise acted upon, so that they are broken up and their pigment deposited about as mementos of their existence. In this fact, the removal or alteration of effete blood, we may find an explanation of the increased size of the spleen. It is easy to understand that under such circumstances we should have alteration in the splenic tissue, probably of an irritative character, the effect of which would be to cause chronic changes in the organ.

The microscopic examination, therefore, of the spleen would show that it has an important function in getting rid of pathological blood, or blood under abnormal circumstances.

If /

If such pathological haemolysis take place in the spleen, we should expect to find certain changes in the liver according to experimental evidence, and observations in other conditions. Now in blood destruction, pigment may be deposited in the liver in two situations; (a) in the capillaries; (b) in the liver cells. Hunter (31). The former is a process going on in the physiological disposal of pigment, and is slow in character, while, when the haemolysis is rapid, or as we may say, pathological, there may be deposit of pigment in the form of minute granules in the liver cells in certain regions. That this is a marked feature in pernicious anaemia there is no doubt, and its occurrence is now common knowledge. The researches of Hunter (34) strongly demonstrate the haemolytic nature of this disease, and were splenic anaemic also a disease depending on pathological blood destruction, or at any rate having such a destruction as its most striking character, we should expect to find some deposit of pigment in the liver cells. Now it has been shown already that the amount of pigmentation of the liver cells, especially in those of the outer two-thirds of the lobules, may be very marked on examination /

examination of sections treated both micro-chemically and by ordinary staining methods, as already described and figured. We have seen that in the two cases examined by myself, there was considerable difference in the amount of pigment deposit in the liver; in one, (Case XII), the quantity was extreme, perhaps more so than in any case of pernicious anaemia, while in the other, (Case I.), although distinct it was not in any way comparable to that in the first. This fact is interesting, and, I think supports Hunter's position as to the secondary role of the liver. This writer says that the quantity of pigment in the liver is no index of the amount of haemolysis, but only shows that a certain quantum of haemoglobin has been broken up within the liver cells, and that it conveys no information as to where the haemolysis took place. Now in these two cases, the pigmentation in the spleen differed greatly in amount, being most abundant in this organ in Case I., where the liver contained very much less, and less plentiful in Case XII, when the liver was loaded. In the former case, the haemolytic process had been more severe, the patient dying marasmatic. Now if the destruction of blood in the spleen was /

was here more severe, (and the fact of finding many large cells containing red blood corpuscles is additional evidence) it is possible that not only the haemolysis itself, but also the breaking up of the haemoglobin both took place in the spleen; hence the very much more marked changes in that organ, with considerable deposit of pigment as compared with the spleen in Case No XII. Reference to this case will show that the duration was much longer, and that the patient's death followed closely on parturition. It is justifiable to suppose that here the haemolytic process was perhaps less severe but more prolonged, the haemoglobin being probably conveyed to the liver more regularly, and being there broken up, and blood pigment being deposited in the liver cells as already described. In the spleen in this case I have not been able to find any certain evidence of enclosure of red blood corpuscles by large cells, as in the other, a fact of considerable significance. Now, had the liver been the chief haemolytic organ as was formerly, and, still is, held by some, we should naturally expect to find the most marked changes in that organ. In these instances it is obviously otherwise, showing that its function in the process of pathological haemolysis is probably the secondary /

secondary one of disposing of the pigment.

Lastly, we may refer briefly to the presence of iron pigment in the epithelial cells of the convoluted tubules of the kidney. The fact is, I think, of some value as evidence of blood destruction, and has been observed in pernicious anaemia. Why the pigment should be deposited in this situation is not clear; it, of course points to the renal epithelium as being the active agent, and the same condition has been artificially produced by injecting iron salts into the blood (36). On the other hand, in paroxysmal haemoglobinuria the glomeruli are the active agents. Probably, some difference in the constitution of the pigment compound is the cause of the difference. Whatever be the explanation, the presence of pigment in this situation points rather to an extensive breaking up of haemoglobin.

From these investigations into the clinical and pathological features of splenic anaemia, we have, I think, ample evidence in support of the proposition given above p. 116, for we have found certain changes in the blood which point definitely to a severe anaemia, and we have seen that these changes are more marked at special times when other conditions arise.

We /

We have, in studying the urine, found that special characters are presented by it when the blood changes are going on, namely, the presence of a considerable quantity of pathological urobilin, or even in very intense attacks, methaemoglobin, and even the presence of corpuscles containing yellowish-brown pigment in the urine. We have remarked the fact that the patients at such times may be 'jaundiced', but that during the intervals they present the appearance of anaemia more or less severe. In the examination of the various tissues, we have found records of changes in the blood which all point to these latter as being destructive, there being, in some situations, evidence of that process in activity, in others the result of blood disintegration in the form of pigmentary deposits in certain organs. Such then is the evidence in support of the intermittent haemolytic theory of the disease.

We may now endeavour to find the cause of this pathological haemolysis.

Researches into the pathology of haemolysis have shown that it may arise under various conditions and may have various seats, and on this latter point depends, so to speak, the general clinical features of the /

the case. As shown by Hunter (34) haemolysis may take place in the portal circulation only, or in the general. Under ordinary conditions, it takes place in the former, while in certain diseased states, the blood may be broken up in the tissues generally, or in the portal circulation to an exaggerated extent. In the cases where the seat of haemolysis is the general circulation, haemoglobin may appear in the urine, and of these, paroxysmal haemoglobinuria is the type, while the others are represented by pernicious anaemia, and haemoglobinuria does not occur. There are, besides this, many and important points of difference between the cases in which pathological haemolysis takes place, according as this process has its seat in the portal circulation or in the general. The presence of pigment in the liver and spleen is the chief evidence that the portal system is the seat, and haemoglobinuria that the general circulation is so in the two diseases mentioned. Now in splenic anaemia, we have the same process of haemolysis, accompanied by the same anatomical changes in the liver and spleen. We may, consequently, conclude that the seat of blood destruction is the portal system. So far, therefore, we /

we have reason for believing that in splenic anaemia, we have a disease of which the essential is pathological haemolysis, and that this process, as in pernicious anaemia, is one going on in the portal system. But this is not all, for in some cases, we may have haemoglobin appearing in the urine as in Cases IV, XV, XVI. How does this fact agree with what has been said as to the seat of haemolysis? For the answer to this question we must again refer to the researches of Hunter already quoted (34) (p.656) and there we find experimental proof that the presence of certain haemolytic agents in the blood in small quantities, will cause the blood destruction to take place in the portal system only, while, with a greater dosage, the changes are no longer confined to the portal, but overflow, as it were, into the general circulation. The haemolytic agent in this particular instance was pyrogalllic acid. Now, it is under precisely similar circumstances that we find haemoglobinuria occurring in splenic anaemia - when there has been an unusually severe attack. By analogy, therefore, we may suppose that, under such circumstances, the haemolytic changes extend from the portal system, this /

this being due to the presence, in greater quantity, of some haemolytic agent, thus causing the breaking up of blood corpuscles and liberation of haemoglobin to take place over a very extensive area. It does not necessarily follow that because the seat of haemolysis is the portal system, that a haemolytic agent is not present in the blood generally; and in the general vascular changes present in this disease, even in those cases where haemoglobin has not been a feature, we have evidence of some general toxæmia, causing general thickening and other lesions in the capillaries and smaller vessels. In support of the supposition that there may be such a general condition, there is experimental evidence, for the injection into the general circulation of certain haemolytic agents may bring about blood destruction in the portal system only (Hunter (34) p.656).

In addition to the changes in the liver, suggesting that the haemolysis is portal, there is further evidence in the severe gastro-intestinal symptoms that there is some special process at work in this system.

Additional evidence of some toxæmia is found in the temperature records, for the very decided pyrexia during /

during the attacks, which we may now speak of as haemolytic, points strongly to the fact of there being present some agent capable of causing not only the blood destruction, but acting as so many other toxic substances do, in producing fever.

Moreover, a very significant fact is the extreme prostration and weakness which have appeared as prominent features in these cases. These symptoms cannot be adequately accounted for by the mere anaemia, for in other cases of anaemia, even with oligocythaemia of greater degree, we do not find the same severity of constitutional disturbance; thus, a case of splenic anaemia with 3,500,000 red blood corpuscles and 30 per cent or 40 per cent haemoglobin will show much more severe and general derangement than many cases of secondary anaemia with the same blood value. We are driven, therefore, to conclude, that in this disease there must be some special substance present in the tissues, which causes destruction of the blood and acts as a general toxic agent.

When, however, we endeavour to discover the nature of this substance, we are at once met by many difficulties which it will require much research to overcome /

overcome. So far, therefore, we can only speak generally, and, by the help of recent investigations into various conditions of pathological haemolysis, try to throw some preliminary light on this obscure problem.

We might naturally suppose that the urine would yield important information as to the nature of the supposed toxine. It is, however, disappointing; so far I have not been able to obtain any evidence on this point.

Can we gain any assistance from the researches of Hunter into the causation of pernicious anaemia? As shown by this writer ⁽³⁷⁾ (p.82.) there are, in this disease, alterations in the excretion of sulphates; that the combined sulphates occurred in greater proportion to free H_2SO_4 than in health, putractive changes in the intestine were in excess. We know that in certain intestinal conditions, this is a frequent effect; aromatic sulphates then being increased, and may appear in the urine. Now in the cases under consideration, I have been unable to find any definite changes in the quantity of sulphates excreted, and, never at any time have I succeeded in finding /

finding such bodies as indoxyl or skatoxyl sulphate of potash present. On some occasions, as already mentioned, such substances were apparently found on previous occasions, but personally many samples of urine were tried under all the various conditions of the disease.

Hunter has succeeded in demonstrating the presence in the urine in cases of pernicious anaemia of ptomaines or nitrogenous bases, such as cadaverine and putrescine. As is now known, these bodies may be isolated from putrifying meat, and have also been discovered in the urine and faeces in cases of cystinuria (38). These bodies Hunter takes as evidence of changes going on in the alimentary tract, due to the action of certain pathogenic organisms, for as now shown by several observers, these bases are the product of their action, and do not appear to be in themselves of poisonous nature. Hunter's theory is, therefore, that under certain conditions, pathogenic organisms of special nature may cause the formation of specific poisons, which are "absorbed from the alimentary tract, the more stable and less toxic being excreted at the same time in the urine" (Hunter, op. cit., p.83). This author would see, in various abnormal /

abnormal conditions of the gastro-intestinal tract, a predisposition to the development of such specific organisms. Hence he suggests that, in malignant disease, in various forms of parasitism, etc., these organisms are enabled to obtain an entrance and multiply, thus giving rise, by a toxaemia, to the anaemia so often observed in such cases, and which may closely resemble pernicious anaemia in their clinical course, and even to some extent in their morbid anatomy, that is, if we are to consider this as a special disease.

Can we apply this theory to splenic anaemia?

There is certainly much to be said in its favour. On the other hand, there is much evidence against such a pathenogenesis. We have seen the long course which many of these cases run as compared with pernicious anaemia, and the various circumstances under which the disease may arise, but of most importance is the distinct hereditary history, which, as we have seen has been a notable feature in three series of cases (vide tables I, II, III).

In these we have the disease arising in very different surrounding circumstances and at different ages, /

ages, and running a very prolonged course. In many of these cases, there has been no antecedent history of other gastro-intestinal diseases, such as would afford a suitable field for the development of specific micro-organisms on Dr Hunter's theory. When gastro-intestinal troubles have arisen, it has been either after the development of anaemic manifestations, or else in conjunction with them. Whether or not pathogenic organisms may be the cause of pernicious anaemia remains to be proved, but the probability is, that in splenic anaemia we have a very different condition of affairs. In explanation I venture to suggest the following theory -

In splenic anaemia, there is a special pathological defect in the gastro-intestinal processes, whereby certain effete products are formed. These on being absorbed, act as haemolytic agents and gastro-intestinal irritants, producing directly and indirectly the various symptoms already described -

If we can accept this theory, we have at once an explanation /

explanation of many of the phenomena. We know that certain constitutional tendencies manifest themselves in the anabolic and katabolic processes and that such tendencies are hereditary, as for example gout, diabetes mellitus (39. p.30 and 40, p.741) and others. In splenic anaemia, we may possibly have an instance of the hereditary tendency to faulty metabolism of a special kind, so that certain substances may be formed, probably in the course of proteolytic digestion in the intestine. We know, for instance that during pancreatic digestion, there are formed bodies such as leucine, tyrosine, hypoxanthine, amido-valerianic acid and others, which are produced independently of the presence of bacteria (41 p.660). It is probable that under pathological conditions we may have the formation of other compounds of the amine and amido series. Under such circumstances, it is easy to see how such substances may have an extremely pernicious effect on the economy, an effect which is well illustrated by the injection of toluylendiamin as described by Hunter, this substance being nearly related to many of the probable products of proteolysis. This substance - the diamine of toluylene C_6H_5
 $C H /$

C_6H_5 is a substitution - derivative in the benzene series C_6H_6 , and many others occur in the process of normal digestion, such as phenol $\text{C}_6\text{H}_5\text{O}$, pyrocatechin $\text{C}_6\text{H}_4(\text{OH})_2$ (which are probably products of proteolysis independent of bacteria) and others which appear as the benzoyl series. Closely related to this is the oxybenzoyl group containing salicylic acid $\text{C}_7\text{H}_6\text{O}_3$. If in this last substance, two atoms of hydrogen be replaced by hydroxyl, we obtain gallic acid, $\text{C}_7\text{H}_6\text{O}_5$ (Dihydroxysalicylic acid); this on heating gives C_6O_2 and tri-hydroxylbenzene or pyrogalllic acid $\text{C}_6\text{H}_3(\text{OH})_3$, which is a well-known haemolytic agent. One could multiply instances of the near relationship of known haemolytic agents to the usual effete products in the process of (pancreatic?) digestion, but this is not the place to do so, and those just given suffice for our purpose, and serve to show how any alteration in the normal chemical processes of digestion may result in the formation of compounds which, differing only in substitutions from the usual products, are nevertheless capable of causing very grave effects by their absorption. It may be also that the formation of unusual substances may explain /

explain the absence of certain bodies from the urine in cases such as those now under consideration.

Can we obtain any anatomical evidence that such changes may take place in the intestine? Many recent observations and experiments on the pancreas, go to show that it has other functions besides ^{that} of secreting ^A pancreatic juice; that in fact, it has an important influence on the general process of metabolism, and perhaps especially on the chemical transformations of the intestinal contents in addition to its action by reason of its ferments.

Now as we have seen in the account of the morbid anatomy of the two cases as given above, there were very obvious changes in the pancreas, the organ in each instance being cirrhotic and showing microscopically definite changes in the gland cells. It is of course impossible, in the absence of full details in a greater number of cases, to say whether such changes in the pancreas are the rule or not, and if they are, whether they are primary or secondary. Still the fact remains that in two well-marked cases, a similar lesion was found, and that in these we have a certain amount of evidence to show that there is a serious /

serious defect in the metabolic process going on in the intestine. Our knowledge is still defective as to many of the changes which may be brought about under different conditions of the digestive glands, so that it is impossible to do more than surmise as to the probable explanation of abnormal effects, but when we know that the injection into the circulation of a substance nearly related to the usual products in the course of digestion is capable of producing severe haemolysis, we are in a manner driven to see some relation between this circumstance and an haemolysis taking place in the presence (in some cases at any rate) of disease of an organ, part of whose function is to form compounds of the same series.

If the absorption of some substance (the nature of which can at present be only a matter of surmise) from the intestinal surface, take place, it would probably produce an haemolysis in the portal area. If more severe, there might be an extension to the general circulation as has been already considered. So we should have produced all the various phenomena accompanying such a process. This does not of course mean that only the blood in the portal system may be affected /

affected, for as already shown, an haemolytic substance may be injected into the general circulation but blood destruction only take place in the portal. Now we have seen that the general circulation may show the presence of some irritant from the fact that general symptoms may be severe, while examination of the kidneys shows marked change (p. 91). We may now turn to the consideration of another important fact - the state of the suprarenals.

It is curious to find that Krukenberg (42) discovered the presence of pyrocatechine or a closely allied body in the suprarenals of herbivorous animals, and we have just considered this as occurring in (pancreatic?) digestion. MacMunn (43) has also shown that haemochromogen is also to be found in these organs. This he considers points strongly to the fact that the suprarenals have for their purpose the excretion of 'worn out or effete colouring matters with their accompanying proteids'. Now if the adrenals are diseased, we should find evidence of the fact in the presence of abnormal pigments in the urine. This has been the case, for in these conditions it is that urohaematoporphrin, pathological urobilin, etc., may appear /

appear. These facts suggest that the suprarenals are blood-metabolising organs, supplementary it may be, but in any case, serving an important excretory function, or else the equally important one of causing some metamorphosis in some proteid substances of poisonous nature, so as to render them inert. The recent investigations of Abelous, Charrin and Langlois (44) strongly support this hypothesis. Now if certain products of proteid disintegration, together with products of haemolysis are present in the blood, we have in the presence of pyrocatechine and haemochromogen in the adrenals, an instance of each being separated by these organs. If too, they are present in increased amount, or if other like products but perhaps of a more toxic nature, are present, we can well understand that there would be increased function on the part of the suprarenals; it might also be that under these circumstances, these organs might themselves become diseased, much as the kidneys do in the case of gout, diabetes, etc. This is strongly supported by the discovery of very marked suprarenal disease in some of the cases I have quoted, while it will be remembered, pigmentation was a remarkable feature /

feature in others. The explanation probably is, that at first the suprarenals are able to carry on their function, that later, as the disease advances, they become inefficient, and whether from failure to excrete proteid poisons, or to render them inert, these remain in the circulation and produce the extreme asthenia which, we have noticed as a character of the disease. That this asthenia is due to toxic effects brought about by inefficient suprarenals, there can now be little doubt in the view of the investigations referred to.

From the fact that the suprarenals have not presented naked-eye lesions in some cases, while in one of those examined by myself, one organ was only partially affected (p. 88) and (Plate IX, fig.2), it would seem that the lesions are secondary, which would support the theory just given. This would also account for the slight pigmentation or bronzing of the skin as compared with that of what we must still call Addison's Disease, for if the organs are wholly affected, and, so to speak, in a primary manner by tuberculous processes, we should get much more marked effects, such as a typical case of Addison will show.

Such /

Such is, I believe the pathology of splenic anaemia. That there is much against the theory I have given is very probable, but it seems in many points to offer a solution of some of the difficulties, is more in accord with recent investigations in haematology, and also lends support to several questions in pathological haemolysis. It also serves to mark the difference between certain diseases which there is some tendency to group together.

Before ending this chapter, we may consider shortly the probable relations and position of splenic anaemia. We must acknowledge its close relationship with pernicious anaemia if we are to consider that as a distinct disease as Hunter does; or if, as many do, there are several anaemias to which the term 'pernicious' may be applied, then probably that called splenic would most justly be considered as pernicious splenic anaemia. We cannot here discuss all the evidence in favor of looking upon one disease as pernicious anaemia. For this the reader can refer to Hunter's paper (45). That splenic anaemia differs from that in its course, morbid anatomy and probable pathology the account now given will, I think, show, though /

though it points out, at the same time, the connection between the two. We also see that a remarkable relation exists between this disease and Addison's, and when taken in connection with recent investigation, throws, I think, a side light on that still obscure disease. What the relation may be between those cases of rachitic enlargement of the spleen accompanied by anaemia, as seen in children, it is not easy to say; this would necessitate a full consideration of the question of rickets, from the point of haemogenesis and haemolysis, but from comparison of the splenic lesions in rachitic enlargement and splenic anaemia as well as the etiology and course of the two diseases, I do not believe they are of the same nature. §

I have examined the spleen and other organs in cases of rickets with enlarged spleen, and have failed to find the sclerosis of the Malpighian bodies, and the endarteritis which are so marked in the spleen of splenic anaemia. Nor have I found pigmentation of the liver cells as in this disease. Clinically, so far as my experience goes, the rachitic cases do not show /

§ Dr.Thos.Barlow (private communication) does not think there is any connection between them.

show attacks of pyrexia with evidence of blood destruction accompanied by increase in the size of the spleen. Any elevation of temperature which such cases may show seems to be due rather to lung complications, and to be quite independent of any haemic condition.

The opinion held by some that splenic anaemia is a splenic form of Hodgkin's Disease, is a somewhat more difficult one than would appear at first sight. As already mentioned (p. 110) this is the conclusion come to by Banti (12) (p.105) § . I was at one time inclined to take this view, but further investigation has failed to support it. As we have already seen, the spleen on section may show a firm, dark red surface, on which it may be difficult to find any Malpighian corpuscles by naked-eye examination; in some cases the section may show some more fibrous areas, but the suet-like appearance of the spleen of Hodgkin's Disease is not found, and instead of there being hypertrophic Malpighian corpuscles, these are very small; and may be completely converted into fibrous tissue.

There is no alteration of the lymph glands, as in adenia, nor has there been found any deposition of adenoid /

§ "Posso formulare in maniera più precisa il mio pensiero dicendo che l'Anemia Splenica non è altro che la forma splenica pura della Pseudoleucemia."

adenoid tissue, in other organs such as the liver. The intestinal tract does not show any lesions similar to those sometimes found in that disease, there being no enlargement of the lymphoid structures of these organs, nor indeed anywhere in the digestive tract. The thickening of the intestine, sometimes present, seems to be due to increase of fibrous tissue in the submucous coat as already described. The condition of the blood seems to be different in the two diseases - for, at first at any rate it does not seem to show any alteration in Hodgkin's Disease, while in splenic anaemia, as we have already observed there is an oligocythaemia from the very beginning. Nor in the latter disease, so far as may be ascertained from the cases I have collected, is there any increase in the number of white corpuscles as may be seen in adenia at some stages. I have examined several cases of lymphadenoma for the purpose of making comparisons between the blood in the two diseases, and have been unable to find similar changes in that and splenic anaemia, in which as well as oligocythaemia, there were more or less corpuscular alterations, as well, though I admit these were sometimes very slight. Clinically, /

Clinically, the two diseases seemed to be quite different, and this opinion is held by others (24). It is supposed by some that the splenic condition may precede the general glandular involvement for a very long time; that is to say, that cases of splenic anaemia, if kept under observation, will ultimately show the essential features of lymphadenoma; in support of this a case of Gretsels' (quoted by Banti (12) (p.58), is brought forward - This was a female child, aged ten, who suffered from an enlarged spleen with anaemia, who, after some time, showed increase of size in all the lymph glands. I do not think this has any bearing on the subject for it is stated definitely that this patient was rachitic. It is much more probable that the girl became the subject of unquestionable lymphadenoma, the original splenic condition being due to the rickets. Also against this theory is the fact, that in some of the cases I have collected there is a history extending over many years, during which time one would expect the glandular involvement to supervene, were it going to do so.

CHAPTER VIII.

D I A G N O S I S .

During life, cases of splenic anaemia have to be differentially diagnosed from the following diseases :

Malaria.
Leucocythaemia.
Hodgkin's Disease.
Rickets.
Syphilitic enlargement of the Spleen.
Pernicious Anaemia.
Addison's Disease.
Enlarged Spleen of Hepatic Cirrhosis.

It has frequently been supposed that the enlargement of the spleen was malarial. In the great majority of cases, there is absolutely nothing to indicate any exposure to such infection; in only one of the cases I have collected (No.XXV) was there a history of ague, and in this instance it was ten years previous to the development of anaemia. The febrile attacks of splenic anaemia bear no resemblance to those of malaria, for although there may be rigors, we do not find the cold, hot and sweating stages as in the latter disease. Nor do these attacks recur with the periodicity of intermittent fever, for, as has been shown in the account of the clinical course, there may be /

be long intervals between febrile attacks, and when these do occur they run a course differing in character, duration and decline, from malaria.

Asthenia, so remarkable in splenic anaemia, is not a feature in cases of malaria, for which it might be mistaken; thus, cases of paludism which develop malarial cachexia with its various complications, are precisely those where a definite history can be obtained, and in which the surrounding conditions are obvious; it is the exceptional cases of malaria, which may be occasionally met with, that give rise to any difficulty, and these do not reach the same degree of asthenia that would make them resemble splenic anaemia, in which this is always a well marked condition at some time.

In the examination of the blood, we have marked differences between the two conditions, for on no occasion have I found pigment-bearing leucocytes in splenic anaemia, nor is there any record, so far as I am aware, of such being found. Nor have any micro-organisms or structures resembling the haematozoa, which have now been fully described by Laveran as occurring in the blood of ague patients, been found. Lastly, the action /

action of drugs is almost absolute as a diagnostic, for quinine fails to produce any effect, or at best, a merely temporary one, in splenic anaemia. A consideration of these facts will probably prevent any error.

Notwithstanding the almost constant mention of leucocythaemia in connection with splenic anaemia by the majority of observers, and their theories as to the relationship between the two diseases, it seems hard to imagine their being confounded when careful examination is made. The absence of increased numbers of white corpuscles, and more particularly, of the special varieties which recent observations have shown to be an important factor in the diagnosis of leucocythaemia, marks the difference between the two. The form, too of the splenic tumour is different, as already indicated.

The question of Hodgkin's disease has already been referred to in the chapter on Pathology, but here we may mention as additional facts for the clinical diagnosis, the different size and shape of the spleen. We need not recapitulate the other points.

The cases of enlarged spleen with rickets offer some difficulty, especially as there is a tendency to call /

call them splenic anaemia. These cases have already been considered in a previous chapter from the point of view of their pathology, so it only remains to point out that splenic enlargement, if accompanied by deformity of the chest, enlarged ends of the long bones, and the other well-known signs of rickets with the usual history, will probably be of rachitic nature, will run a different course, with a different prognosis, and will therefore constitute a separate condition, and one not to be confounded with splenic anaemia.

Syphilitic enlargement of the spleen may, in some cases, perhaps, offer some difficulty, especially, if to a certain amount of anaemia, a sudden enlargement of the spleen should take place, I have seen this occur in one case where the spleen became dislocated and twisting round, caused its pedicle to kink, giving rise to great enlargement of the organ with increase in size. At first sight, a case like this might lead to a mistaken diagnosis, but the history and presence of signs of syphilitic ulceration, etc., will generally reveal the true nature of the case.

Pernicious Anaemia.

We /

We have already discussed the possible relationship between this disease and splenic anaemia (p.150). If however we grant that pernicious anaemia is a distinct disease in itself, we may still have some difficulty in making a clinical diagnosis, for there is much similarity in the appearance of patients suffering from both. As a rule, however, there is no splenic enlargement in pernicious anaemia, or if this organ should be increased in size, it is not to the same extent as in the other, nor does it offer the same characters of a firm, tense, well-defined tumour reaching to, or beyond, the umbilicus. The duration of the two diseases may be different, for, as we have seen, we may find a history, in cases of splenic anaemia, extending over several years, and on the whole running a very different course from those of pernicious anaemia. In the blood, too, we find valuable information, for in pernicious anaemia, the changes are much more pronounced, oligocythaemia, poikilocytosis, and corpuscular nucleation are all more marked than in splenic anaemia, where, as we have seen, reduction in the number of red blood corpuscles may be the only change at all evident; or if there be poikilocytosis present, /

present, it is generally to only a slight extent as compared with pernicious anaemia. Therefore, the history, physical signs and condition of the blood must be our guides as to differential diagnosis.

Splenic anaemia differs from Addison's disease proper in the small amount of pigmentation, the presence of splenic and usually hepatic enlargement, and the condition of the blood. As regards the last, in cases of Addison's disease where I have examined the blood, there was oligocythaemia to some extent, but even in advanced stages I failed to find any other changes. There would, however, be great difficulty in distinguishing cases of Addison's disease with enlarged spleens from splenic anaemia. That such cases do occur is a fact, and in connection with what has been said as to suprarenal lesions, we may well ask, is differential diagnosis called for?

The enlarged spleen of hepatic cirrhosis should offer no difficulty, for the collections of fluid, more or less extensive in the peritoneal cavity, the diminished hepatic dulness usually present, with well-defined superficial veins, together with the history, will generally distinguish the liver affection from the /

the anaemia.

Other causes of enlarged spleen as lardaceous disease, hydatids, etc., need no mention.

In conclusion, a patient presents a marked anaemic appearance, with asthenia, attacks of vomiting, diarrhoea, irregular pyrexia at times and, it may be, epistaxis or some other haemorrhage; together with these symptoms, a considerable enlargement of the spleen, but no increase in size of the lymph glands; and, as to the blood, oligocythaemia, with a tendency more or less to poikilocytosis, the white corpuscles being unaltered. These conditions in the absence of a rachitic history, point to the diagnosis of splenic anaemia.

CHAPTER IX.

P R O G N O S I S.

From what has been said, it is plain that the outlook is serious. At the same time, the history of the many cases given in this paper makes it evident that the prognosis is not so bad as Müller and others would make out, and Banti's statement (12). (p.107) that the disease runs a more or less rapid course, must be considered as erroneous, for, in the chapter on duration, we see the disease may extend over many years. In the early stages, therefore, we may hope for considerable improvement with capability for work in the intervals of the attacks which form such a salient feature in the course of the disease. When, however, the patient suffers more severely from prostration, with complications such as ascites, severe epistaxis, etc., the prognosis is that the disease is gaining ground. Examination of the blood at this time is the chief indication, for if the number of corpuscles and amount of haemoglobin rise with the subsidence of pyrexia, jaundice, and diarrhoea, the probability is that there may be a fair restoration to health. On the other hand, if the haemoglobin and /

and corpuscles show little change for weeks after an attack has passed off, if prostration continues with epistaxis, purpura and other symptoms of considerable constitutional derangement, it may be concluded that the disease will make uninterrupted progress, and that at no far distant period, the patient will enter the marasmatic stage. Intermittent temperature, profound anaemia, severe vomiting and diarrhoea point to a speedily fatal issue.

CHAPTER X.

T R E A T M E N T .

Treatment is unfortunately very unsatisfactory, and there is not much to be said concerning it. On the supposition that the disease was malarial, quinine has been tried in many cases. In most instances where used, the drug has done no good, and even actual harm in some, as in the cases recorded by Dr Wilson and myself, when it had the effect of causing nausea and vomiting. A variety of drugs have been tried, such as strychnine, and the various vegetable tonics, mercury, iodide of potassium, the different iron salts, and arsenic. The last is the only one which has produced any beneficial effect, being given in the form of liq.arsenical. As in other anaemias, and so far as my own cases are concerned, it has certainly improved the patient's condition; in others, however, it has failed and indeed seemed to be injurious, as it started diarrhoea of a severe form. Iron does not appear to do any good.

In one case, (No.III), intestinal antisepsis in the form of x-grain dozes of salol thrice daily was tried, but the result was doubtful and I have not had another /

another opportunity of trying its effect.

During the febrile attacks antipyrin has certainly been of service not only reducing the temperature but relieving the splenic pain, and giving sleep.

Besides drug treatment, electrical means have been tried as faradization of the spleen, galvano-puncture, etc. They have all been disappointing.

Transfusion has been tried in some cases, and is recommended by Strümpell when the anaemia becomes severe towards the end of the case, or if there has been severe epistaxis or other haemorrhage. It has not been employed in any of the cases I have seen, but the opinion of those who have performed it is that no good effect results except perhaps after haemorrhage.

On the grounds that the spleen was the organ primarily at fault, splenectomy has now been carried out in several cases. Banti's table(12 pp. 116-117) of cases of excision of the spleen does not by any means support the favorable way in which he speaks of it § . The only case which I have known anything of, personally, was the aunt of the patient, Case No.IV, whose /

§ Vide supra. p.115 for criticism of this table.

whose spleen was removed by Dr Savage of Birmingham, but, although she got over the effect of the operation, the case ended fatally in a short time. Moreover, if the disease affect the spleen secondarily, as is maintained in this paper, to excise the organ is surely illogical, for, if we may suppose its action to be that of abstracting from the circulation blood which has become pathologically altered, its removal cannot but have an injurious influence on the case. On the whole, splenectomy does not seem justifiable.

Diet is of importance, for highly nitrogenous foods are injurious in the presence of pathological haemolysis, consequently a bland, but at the same time, as nutritious a diet as possible must be recommended. It must be borne in mind that the pancreas has been found cirrhotic, so any foods which would call for increased activity on the part of that organ, would be unsuitable.

From what has been said as to possible intestinal changes, it is obvious that all attention must be paid to the excretory functions.

A point of great importance, is to avoid exposure to cold, for in many instances, a chill has brought on /

on an attack of haemolysis . The general indication therefore is, to raise the patient's general health to as high a standard as possible, so that there may be increased haemogenesis, and to take care that anything which might promote blood-destruction be avoided.

CHAPTER XI.

C O N C L U S I O N S.

From the account of Splenic Anaemia as here given, we may draw the following conclusions :

(A) As to its Etiology, we find :

(1) It may have a hereditary tendency, extending over, at least, three generations.

(2) Apart ^{from} heredity, it may arise under various conditions, as regards social position and occupation; it may perhaps be favoured by starvation, overwork or pregnancy, but the evidence of this is uncertain.

(3) It may appear at any age, and is not, by any means, a disease peculiar to children.

(4) It does not appear to have any connection with rachitis or syphilis.

(5) There is nothing to warrant its being due to malarial infection.

(B) As to its Clinical Course :

(1) The disease may begin insidiously and cause progressive anaemia and debility. There is subsequently developed very marked anaemia, a

peculiar tint of the skin, considerable enlargement of the spleen and generally of the liver, without change in the lymph glands.

(2) The blood shows more or less reduction in the number of red corpuscles and haemoglobin, the white cells being unaltered; there may be a certain amount of alteration of the red corpuscles themselves.

(3) The urine shows peculiar characters, containing abnormal constituents.

(4) There is a peculiar temperature, pyrexia of an irregular kind being present at one time or other, and haemorrhages are frequently observed.

(5) There may be intermission of almost all the symptoms for periods of variable length during the earlier stages.

(6) A marasmatic stage is finally developed.

(C) The duration may be from a year to many years.

(D) The Prognosis :

(1) In the earlier stages this is good, for subsidence of symptoms generally occurs.

(2) The ultimate prognosis is bad, the patients usually dying from marasmus or some intercurrent disease.

(E) As to the Morbid Anatomy, we find:

- (1) Well defined changes in all the organs connected with the haemic system, as the spleen, liver and bone marrow.
- (2) Remarkable changes in (some cases) in the supra-renal bodies.
- (3) Lesions (probably secondary) of the intestinal tract and blood-vessels.
- (4) In some cases, cirrhosis of the pancreas.
- (5) An absence of changes in the lymph glands.

(F) As to Pathology, we may conclude :

- (1) That the main condition is pathological haemolysis.
- (2) That the disease is not a 'primary splenopathy.'
- (3) That we have not to do with a defective haemogenesis.

(G) As to Pathogenesis :

- (1) There is probably the absorption into the blood (of the portal system) of some toxic product which acts as a haemolytic agent.
- (2) The nature of this product is, so far, unknown, but is probably formed in the process of

proteolysis.

(3) Its presence in the blood :

(a) causes destruction of red blood corpuscles

(b) acts as an irritant on other organs, producing structural changes in them.

(H) As to its Nosological Position the disease :

(1) Does not appear to have any relation to leucocythaemia.

(2) It has many points in common with 'Pernicious Anaemia.'

(3) It bears some relation, so far as effects are concerned, to 'Addison's Disease.'

(4) It is probably not a splenic form of Hodgkin's Disease.

It must, of course, be admitted that future investigation may cause us to modify these conclusions, and will doubtless. These cases have, so far, received little attention in comparison with their interest, and therefore much remains to be learned concerning them. This I have endeavoured to do, in the hope that any facts I have been able to collect may help to throw some light on their nature.

C L I N I C A L C A S E S

of

S P L E N I C A N A E M I A .

CASE I.

(From personal observation.)

Enlargement of Spleen with profound anaemia and as-
thenia; no enlargement of glands .

Great reduction in the number of red corpuscles; no
increase in the white.

Skin pigmented.

Diarrhoea; epistaxis; pyrexia; death.

Post Mortem. Hypertrophic spleen, intestinal ulcera-
tion; sclerosis and cyst of suprarenals.

Elizabeth N., age 39, charwoman, widow, admitted
to hospital, February, 1893. Has had 10 children.

Family History.

There is little of note in her family history.
Her father was quite healthy so far as she remembers;
her mother died of 'dropsy'. Her eldest child, age 18,
appears quite healthy; her youngest, age 18 months,
is apparently healthy; the others have had the usual
illnesses of children, some dying of whooping cough,
etc. There is no family history of phthisis nor any-
thing to suggest syphilis.

Previous History.

The patient says she had a healthy childhood, be-
ing brought up in the country. She does not remember
having /

having had any serious illness, and was never considered rickety.

At the time her first child was born, (18 years ago), she first noticed a "lump in her left side". This swelling did not trouble her in any way and remained the same till her admission, (25th February, 1893.) Six years previous to admission she brought up some blood, but after this she remained in fairly good health till three months before her admission into hospital; she was never troubled with cough nor any other indication of chest disease.

Present Illness.

Her actual failure in health began three months before her admission, i.e., November-December, 1892, with great weakness and inability to eat, but there was no vomiting nor diarrhoea. She had a slight cough and complained of aching pains in the abdomen. She perspired freely at night and during the day felt very cold and at times sleepy.

Present Condition.

The patient is fairly well nourished, and of a dark complexion, but appears anaemic, notwithstanding that the cheeks are somewhat flushed; the skin is moist /

moist, the sclerotics pearly.

Alimentary System. The appetite is very bad but there is no vomiting nor nausea nor other particular subjective feature in connection with digestion, but the patient complains of pain and tenderness in the left hypochondrium. The tongue is raw and shows patches of white fur on its surface. There is no enlargement of the tonsils. The bowels are constipated, being moved only about once in four days; the motions are then noticed to be quite black and unformed.

Examination of the Abdomen. There is visible a considerable swelling in the left side of the abdomen, which physical examination shows is the spleen. The organ is very tender on palpation. The liver does not appear to be enlarged.

Circulatory System. Examination of the heart does not show anything notable; the pulse, - 108, showing great variation, the tension being low, pulsations regular.

Respiratory System. The patient has a slight cough. Respirations - 36-40. Examination of the lungs shows faint rhonchi at the left base; there is no friction; the lungs seem otherwise healthy.

There /

There are no enlarged glands to be felt anywhere.

The nervous system shows nothing abnormal; the fundi are healthy. Urine - Reaction = acid S.G. 1010; Urea 2% ; No abnormal constituents.

There is great irregularity of temperature (vide chart) the evening rise being very great at times.

Blood :- R.B.C. = 3,670,000

W.B.C. = 10,000 (circa)

Haemoglobin reduced.

There are no irregular forms of red corpuscles.

Progress of the case.

March 6th 1893. - The patient feels much better though still very weak; the colour is much improved. The spleen though considerably smaller, can still be easily felt. There is still some constipation. The irregularity of temperature continues to be a marked feature. The red blood discs = 3,670,000.

March 27th.- The spleen is again increased in size extending over three inches beyond the costal margin, there being a distinct notch felt. There is no change in the chest condition.

April 17th.- The spleen now extends to about one inch above the umbilicus; there is great breathlessness and the patient perspires considerably.

April /

April 26th. - Blood, examined, shows decrease in red corpuscles, but no increase in the white.

July 6th. - The patient is losing weight (having gained after admission) the spleen continues to increase in size reaching now almost to the middle line of the abdomen, inwards and downwards to a point two inches below the umbilicus.

August 13th. - The spleen has still further increased in size.

August 24th. - The patient had a fit this afternoon which lasted (apparently) about five minutes. It began without any cry; she became stiff; the head was thrown back; the eyes and face twitched especially on the left side; the face became swollen and bluish; she bit her tongue and had foaming at the mouth, and passed urine; the eyes remained open and pupils dilated, and she was unconscious. (Nurse's Report.)

88 grains of urea passed since 23rd.

August 25th. - Patient is very weak this morn; she slept after the fit of yesterday. The urine contains a very faint trace of albumen.

October 2nd. - The patient had another fit last night similar to that of August 24th.

October /

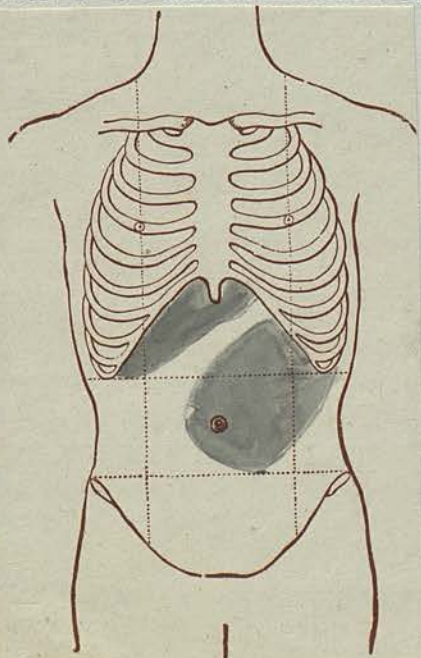
October 8th. - Patient is now suffering from diarrhoea.

October 10th. - There was epistaxis this morning.

Note: This is the record of the case up to the time I saw the patient, on October 18th, 1893, when her condition was as follows:

Condition on Examination.

The patient is emaciated and extremely anaemic. There is a somewhat dusky olive tinge about her forehead, and the general colour of the skin in the flexures of the elbows, the neck, etc., is certainly dark. The mucous membranes are very pale but no pigmented patches are visible. The expression is anxious. There are no bed sores. The appetite is very bad, the patient is troubled with vomiting and retching; there is very severe diarrhoea which is almost incessant and there is incontinence of both urine and motions.



The tongue is dry, denuded at the tip and coated in the middle. Examination of the abdomen shows a distinct and considerable swelling on the left side which is found to be the spleen, greatly enlarged. The margin is sharp and well defined /

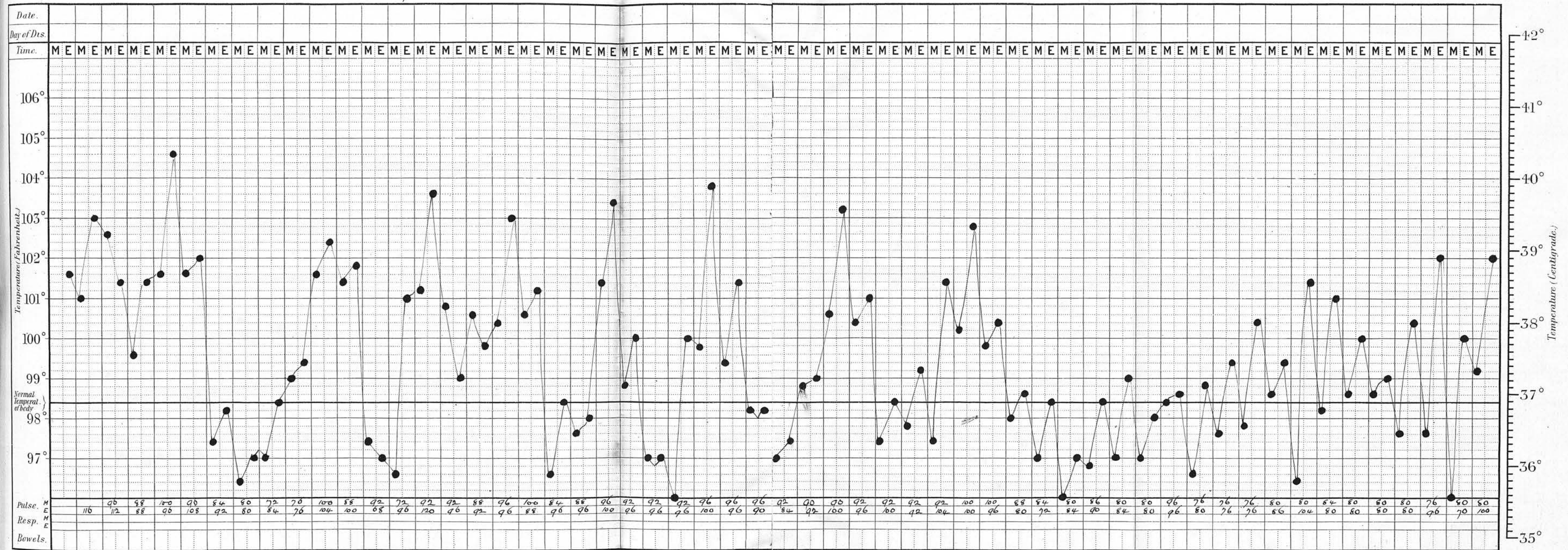
defined and the notches distinct, the general shape being oval. The organ reaches to two inches to the right of the median line and downwards to a point three inches below the level of the umbilicus. There is some tenderness on palpation. There is also enlargement of the liver which extends downwards and towards the spleen; the whole liver dulness being six inches, beginning at the level of the 6th right rib.

Urine:

Quantity	=	40 oz. average.
Colour	=	Dark amber at times, sometimes paler.
Reaction	=	Acid.
Spec. grav.	=	1010.
Urea	=	1-1.5 per cent.
Albumen	=	Present, but not copious.
Blood	=	No reaction.
Bile	=	" "
Sugar	=	" "
Phosphoric acid	=	0.12 per cent.
Chlorides	=	} Appear reduced in amount.
Sulphates	=	
Indoxyl Sulph. K.	=	} No reaction.
Skatoxyl Sulph. K.	=	
Peptone	=	No reaction.
Microscope	=	A few pus corpuscles, granular casts and débris.
Spectroscope	=	Absorption bands of pathological urobilin.

Examination of the heart shows some dilatation of the organ with soft blowing murmurs at the base on auscultation. The pulse = 112, is somewhat irregular, the tension /

Name *Elizabeth N.* Age *39* Disease *Splenic Anaemia* Admitted _____ Age _____ Disease _____ Admitted _____ *to follow p 179*



tension being poor. The respiratory system shows on examination some mucous râles at the bases. There is some cough.

There are no enlarged glands to be found anywhere.

Nervous System.

The patient is sleepless and very restless, and suffers from headache of an indefinite character. There is no sensory abnormality. Motor power is very feeble but there are no paralyses. The knee jerks are very feeble, but present, the superficial reflexes are present. There is no ankle clonus. The organic reflexes (rectal and bladder) are imperfect. There have been only two convulsive seizures as described (vide supra)

The blood:	R.B.C.	=	2,130,000
	W.B.C.	=	15,000
	Haematoblasts	=	113,000
	Haemoglobin	=	10 per cent.

There is slight variation in the size of the red corpuscles, but no nucleated forms are seen. There is no poikilocytosis. There are a very few corpuscles measuring about $3\ \mu$, quite globular apparently and showing no particular structure (Eichorst's?) The white cells /

cells are of the usual forms, measuring about 10 μ , showing mono- and tri-nucleation, and there are a few eosinophilous cells of the normal size and characters, but none suggestive of the abnormal forms seen in leucocythaemia.

Oct 25th. - The patient is much lower and in a marked cachectic condition, extremely emaciated, and of a deeper olive colour than before; diarrhoea, etc., continue.

Blood :	R.B.C.	=	1,620,000
	W.B.C.	=	10,000
	Haemoglobin	=	10 per cent.

Characters as when last examined.

Patient died November 4th, 1893, in a state of marked cachexia.

For Post Mortem Report, vide p,78.

CASE II. (from personal observation).

Intermittent weakness; haematemesis.

Epistaxis; history of jaundice.

Pigmentation of skin.

Enlargement of spleen; no palpable glands.

Decrease in the number of RBC; no increase of the WBC.

Dark coloured urine.

James K., age 21, blacksmith, complains of great weakness.

Family History.

The patient's father is dead; cause of death unknown; the mother died of consumption. He has one maternal uncle, who is healthy, and his maternal grandmother is strong and well. The patient was the only child.

Previous Illnesses.

He has had measles, and often had sore throats. There is no history of syphilis.

Present Illness.

For some considerable time the patient has been subject to periods of great weakness, but he is uncertain as to when this began. In the latter part of 1891, the patient "brought up blood" and also noticed that /

that he passed blood in his motions. This occurred again just before Christmas 1892, and at the same time his abdomen became much enlarged, and he was also troubled with extreme weakness. This condition recurred again in September 1893. On each of these occasions, the patient felt somewhat sick and then vomited dark coloured coagulated blood. On the last occasion, the patient had a return of the haematemesis the following day, and afterwards some vomiting without bringing up any blood, and he felt extremely weak.

Sometime in 1892 the patient had a severe attack of epistaxis, but has not had any other similar attack. He says that after each attack of haematemesis, he suffers from sharp pulling pain in his abdomen, which obliges him to keep quiet.

At present, he feels weak and cannot make any effort.

Present Condition.

September 10th. 1893. - The patient weighs about 10 stone, is sparely built, but has a prominent abdomen; he is very pale with dark eyes, and the general colour is an olive. He is not yellow tinged now, but says that at times he becomes quite jaundiced. The forehead and axillae appear more pigmented than is usual, even with dark skinned persons.

The /

The lips and tongue are pale, the latter flabby,
The appetite is very variable.

There is no pain after food. The bowels move 1-2-3
times per diem. There is no flatulence as a rule.

Examination shows the abdomen to be greatly enlarged, and on moving there is undue prominence between the two recti muscles; the abdomen is not, however, tense. On palpation, there is a considerable tumour felt, extending from under the costal margin on the left side, and extending downwards and inwards to the umbilicus as its extreme limit. The surface is generally smooth, but at one part there is a distinct boss, slightly anterior to the anterior axillary line; this prominence is painful on palpation. The tumour is oval in form and its margin is distinctly notched. Percussion shows it to begin at the left 9th rib in the mid-axillary line and that the dulness is continuous to the umbilicus; in the epigastric region, it does not come so much towards the middle line as in the umbilical. The hepatic dulness measures three inches in the right nipple line, and does not extend to the costal margin. Although the whole abdomen gives some feeling of fluctuation, there is no definite evidence of fluid. Measurement at umbilicus = 37 inches.

Respiratory System. The percussion note is resonant all over, the breath sounds are good, and there are /

are no accompaniments.

Circulatory System. The cardiac impulse is not well defined but is most marked in the 5th left space $\frac{1}{2}$ inch internal to the nipple line. There is no increase of cardiac dulness. Auscultation gives a systolic murmur at the apex which is not, however, conducted beyond the mitral area.

Both in the aortic and pulmonary areas blowing systolic murmurs are heard. Pulse 100, somewhat quick, but regular, tension fair.

Glandular System. No enlarged glands can be felt anywhere; the thyroid does not show any enlargement.

Nervous System. The patient does not sleep well. There is no particular headache; no abnormal sensations. The superficial and deep reflexes are normal. There is no ankle clonus and the organic reflexes are all normal.

Sight is not good (myopic) but there are no changes in the fundus. Hearing is defective in the left ear, good in the right.

Blood :-	R.B.C.	=	3,650,000
	W.B.C.	=	10,000
	Haemoglobin	=	30 per cent.

In Hayem's fluid, most of the red discs are of good average /

average size, and well shaped; but a few are seen considerably above the average size and others show flask shapes and buds. No nucleated forms are seen. The white cells are perfectly normal.

Urine :-	Colour	= dark amber.
	Reaction	= acid.
	Spec. grav.	= 1020.
	Urea	= 2.2 per cent.
	Chlorides	present.

No reaction for albumen, blood, sugar, bile, peptones, indol, skatol.

Spectroscope showed absorption bands of pathological urobilin.

Additional Notes.

September 25th. - The patient is very much worse in every way; there being a considerable amount of fluid in the abdominal cavity (measurement at umbilicus = 40 inches). There is apparently no increase in the size of the spleen, but the organ is much more tender on palpation. There is considerable diarrhoea, but no vomiting; there is also extreme breathlessness and palpitation on movement. The cardiac impulse is displaced upwards to the 4th left space.

R. /

R.B.C. = 3,200,000 Haemoglobin 23 per cent.

October 21st. - Patient feeling much better,
fluid much reduced (disappeared?) from abdomen.

R.B.C. = 3,340,000.

W.B.C. = 10,000.

Haematoblasts = 80,000

Haemoglobin = 25 per cent.

13th January, 1894. Patient much stronger.

R.B.C. = 3,520,000.

CASE III.

(From personal observation).

Progressive Asthenia.Enlargement of Spleen.No Glandular Change.Marked Anaemia.Purpura. Epistaxis.Pigmentation of Skin.

Mrs Annie S., age 33, housewife.

Family History.

The patient's father is alive and enjoys good health; her mother died of "cancer in the womb". She has one sister and two brothers, all of whom are perfectly strong and healthy. The patient has had six children, five being alive and perfectly healthy. The first was born prematurely and lived only six weeks; her eldest child, a girl of 12 is very strong and healthy in appearance, and does not show any morbid condition.

Previous History.

The patient had rheumatic fever 14 years ago, with which she was laid up for some weeks; she does not remember having any other illness. Her confinements have all been good, and she has never had any miscarriages./

miscarriages.

Present Illness.

This began in July, 1893, so far as she is aware; she noticed that the menstrual periods ceased; that she was troubled with morning sickness and vague pains in her legs. At the same time, or even previous to these, she complained of extreme weakness, and that on going upstairs or making any exertion, she very soon got out of breath. Since August, 1893, she has been unable to do anything in the way of work, being obliged to lie down most of the time. In September, 1893, she one day had a bad attack of epistaxis; this came on in the middle of the day; and although it did not last very long, was very severe. In the following December, she noticed that her stomach was very much larger than usual. She says she has never had jaundice. Since these symptoms first began, the patient has been gradually losing weight.

Present Condition.

The patient is very pale but not blanched, spare, expression anxious. The mucous membranes are also pale but do not show any pigmentation. There are, however, distinct pigment spots on the dorsal aspect of both /

both hands, especially the left; vide plate I. p.26
 These the patient says, have appeared recently, and are getting more marked; there does not appear to be any undue pigmentation of the areolae, axillae, etc., the sides of the neck are doubtfully more pigmented than is usual in this class. She is not jaundiced; there is slight oedema of the lower limbs.

Digestive System.

The patient takes food fairly well; there are no subjective sensations, nor is she troubled with vomiting since last summer; the bowels are now regular. There is some gingivitis, the tongue is pale slightly fissured and furred; tonsils not enlarged. There is no distension of the abdominal veins. The liver is enlarged, extending from the sixth rib in the nipple line to about three inches below the costal margin.

Haemic System.

There is considerable enlargement of the spleen almost to the median line at the umbilicus, and downwards to $1\frac{1}{2}$ inch above the level of the ant. sup. iliac spine. The general shape is oval, the margin is rounded, and the surface of the organ feels fairly smooth and palpation is painless; the well-marked notch can be felt. The note is dull on percussion. The thyroid /

thyroid is not enlarged. No enlarged glands can be felt anywhere.

Circulatory System.

The patient suffers from palpitation; the cardiac impulse is visible in the 5th left space and in the nipple line; it feels well defined, even somewhat heaving. The upper limit of the heart begins at upper border of the 3rd rib, the right is at the the right lateral sternal line, the left, in the left nipple line. On auscultation, a distinct systolic murmur is heard in the mitral area and is propagated up to the axilla; it is lost on passing to the right side of sternum, but may be heard at the base. In the aortic area, the second sound is well heard, while in the pulmonary area, the second sound is reduplicated, the pulmonary portion being accentuated.

Pulse 85, regular; tension good.

Respiratory system, negative. The nervous system is also negative. There is no tenderness on percussion of the bones.

Urine	= 24 hours	= 1050 cc. 36 oz.
Colour		= amber, slightly opaque.
Reaction		= neutral.
Spec. Grav.		= 1008-1012.
Urea		= 12.6 grams.
Albumen		= present.
Blood /		

Blood	=	no reaction.
Bile	=	" "
Sugar	=	" "
Chlorides	=	2.62-3.675 grams.
Phosphoric acid	=	0.525-1.26 "
Sulphuric acid	=	2 grm. (approx)
Indoxyl sulphate of k.	=	no reaction.
Skatoxyl sulphate of k.	=	" "
Peptone	=	" "
Microscope	=	Pus corpuscles, squamous epitheli- um, some casts, in which are pigment granules.
Spectroscope	=	presence of patholo- gical urobilin.

Blood :

R.B.C.	=	2,750,000.
W.B.C.	=	10,000.
Haemoglobin	=	25 per cent.

The red discs show some variation in size; many are oval in form, others distinctly pyriform; in fact poikilocytosis is a marked feature; here and there a few of these corpuscles may be seen undergoing fragmentation, with the separation of small masses of a bright colour; no nucleated red discs nor poikiloblasts are seen on this occasion. The white corpuscles do not show any deviation from the normal. A few days later, examination of the blood showed an increase in the number of red corpuscles (3,210,000) and a few showed nucleation,

Progress /

to follow p. 192



(RIGDEN'S CLINICAL CHART.)

Progress of the case.

There is a markedly irregular temperature (vide chart p.192 .) After admission the number of red blood corpuscles seemed to rise, and the patient said she felt better. This improvement was only temporary, for the patient had severe attacks of vomiting, epistaxis and diarrhoea. A copious purpuric eruption appeared on the legs (vide Plate II., p 41.). The number of red corpuscles decreased as also the haemoglobin to 2,200,000, and 20 per cent respectively.

The size of the spleen increased and the patient developed a more wax-like appearance. Ophthalmoscopic examination was always negative.

Salol in x grain doses t.d.s. was tried, and at first seemed to control the vomiting and diarrhoea, but its effect was doubtful. The patient refused to remain longer in hospital.

CASE IV.

(From personal observation.)

Enlarged spleen, with anaemia and asthenia in three generations of the same family.

Pigmentation of the skin.

Intermittent attacks of weakness accompanied by increase of anaemia, diarrhoea, etc.

Considerable reduction in the number of red blood discs; no increase in the number of the white; no glandular enlargement.

Charlotte B., age 34., married.

Family History.

Father dead. The patient states that he was in ailing health as long as she can remember him; she also states that he was always somewhat 'yellow' and was never able to do much as he was 'always weak', he always looked very ill. The 'jaundice' was at times much worse, and when such was the case he generally was very sick and much weaker. He had an enlarged spleen for some years before his death. About nine months before his death, he took to his bed and died in a condition of great weakness. (These details have been verified by reference to the doctor who attended him). The patient's mother is alive, but there is little to be learned about her, except that her family /

family was consumptive. The patient had an aunt on her father's side who had an enlarged spleen. This was considerable, but there were no other features noticed. She was operated on by Dr Savage of Birmingham, who describes it as 'a greatly hypertrophied spleen'. She died some time after. Another paternal aunt living in London suffers from great weakness. Otherwise there is nothing special to be learned.

Previous History.

The patient enjoyed good health as a girl and never suffered from either jaundice or weakness. As a child she had measles and chickenpox. There is no history of rickets nor anything pointing to syphilis. She has never been out of England and has always lived in Birmingham. Up to 18 she had a comfortable home, but from that age to 23 she had to live in lodgings. She is strictly temperate in her habits. The patient married at 23.

Present Illness.

This began about eleven years ago. She became weak and suffered from fainting fits. For this she consulted a doctor who told her 'she had a lump in her side'. After this, the patient suffered much from weakness /

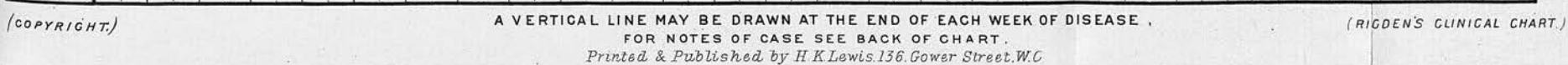
weakness, fainting, pains in her hips and jaundice. The first attack of jaundice was about four years ago, (end of 1889). She was very ill and confined to her bed; she noticed that the water was 'almost black'. She became pregnant in 1890, and during this time she was in very bad health and more or less yellow. Her baby was born in 1891, and lived five months; it had marked splenic enlargement. (This has been verified by reference to the doctor who attended the child.)

After the birth of the child, she had a severe attack of "inflammation" in the region of the spleen. Since then she has suffered intermittently from pain in the left hypochondrium, and diarrhoea.

Present Condition.

The patient is very pale and anaemic looking; hair and eyes light brown. She has a pigmented patch on the back of her left wrist, and several others of smaller size on her right arm, both sides of neck, etc.; these she says are getting larger. There is some pigmentation of the axillae, but the areolae are not darkly coloured. There are no pigmented patches to be seen in the buccal mucous membrane. She is not at /

to follow p 196



at present jaundiced; nor is there any other morbid appearance.

Alimentary System.

Appetite poor, and on taking food, there is a feeling of fulness and pain in the epigastrium and sometimes a feeling of nausea, but no vomiting. The bowels are irregular, the patient at times suffering from severe diarrhoea; at other times there is constipation. The patient has frequently noticed that the motions have been very dark-coloured, even black.

Physical examination.

The tongue is moist and red and somewhat fissured; the teeth are defective; there is no enlargement of the tonsils.

Inspection of the Abdomen shows some prominence of the left side of the abdomen, and on palpation a considerable tumour is felt, which the ordinary procedure shows to be the spleen. The organ extends to $1\frac{1}{2}$ ins. from the median line to left, and down to a point 4 inches above the level of the superior anterior iliac spine. The margin is well-defined and shows a well-defined notch. At various parts of its surface, the spleen is extremely tender so that thorough palpation /

palpation is impossible. There is no palpable increase in the size of the liver, and percussion shows that dulness begins at the 5th rib in the R^t.V.N.L., and extends to the costal margin. There is no dilatation of the stomach. Examination of the kidneys is negative.

Circulatory System. The patient complains of some precordial pain and there is palpitation with dyspnoea on going upstairs.

Physical Examination.

The cardiac impulse is in the 4th left space, $2\frac{1}{2}$ inches from the left lateral sternal line; the impulse is ill-defined and soft; the cardiac dulness begins at the upper border of the 3rd rib in the nipple line, and the right border is about $\frac{1}{2}$ inch to the right of the right lateral sternal line in the 4th intercostal space.

On auscultation, a soft blowing murmur is heard at the apex, systolic in rhythm, and not extending much beyond the apex. The 2nd sound at the apex is very faint. In the aortic area, the 1st sound is not heard, the 2nd is faint; no murmur is heard. In the tricuspid area both sounds are faintly heard. In the pulmonary area, there is a soft systolic blowing murmur /

murmur. There is no exocardial murmur. Pulse = 72, regular, soft, compressible.

Respiratory System. There is no cough, but the patient sometimes complains of severe pain on inspiration in the epigastrium, and at the base of the left lung posteriorly. Physical examination shows nothing abnormal in the lungs except at the left base where the breath sounds are somewhat faint and distant.

Nervous System. The patient complains of bad headache, in the morning, especially. She sleeps badly. There are no abnormal symptoms subjective or objective. Memory and the mental condition are good.

Blood Glands. There is no glandular enlargement to be found anywhere. There is no enlargement of the thyroid. The skin is healthy everywhere except for the pigmentation already described.

Urinary System :-

Urine in 24 hours	= 1450 cc. (54 oz).
Colour.	= dark amber.
Re-action	= acid.
Spec. Grav.	= 1012.
Urea	= 21.75 grammes
Albumen	= present (slightly)
Blood	= no re-action.
Bile	= no re-action.
Sugar	= no re-action.
Phosphoric acid	= 1.88-2.17 grm.
Chlorides (NaCl)	= 3.62-4.93.
Sulphates (H ₂ SO ₄)	= 1.52-1.19.
Indoxyl /	

Indoxyl Sulphate of K. = no re-action.
 Skatoxyl Sulphate of K. = no re-action.
 Peptones = no re-action.
 Ehrlich's re-action = negative.
 Spectroscopic examination shows the presence of

pathological urobilin in fair amount.

The Blood. Repeated examinations have been made

Sept. 23rd	R.B.C.	=	3,266,000
	W.B.C.	=	20,000
	Haematoblasts	=	340,000
	Haemoglobin	=	.38 p.c.

There is some variation in the size of the red discs, some being 4-5 μ , others 8 μ ; there is no deformity, nor are any nucleated cells seen. There are no abnormal varieties of coloured cells to be seen.

The white corpuscles do not show any abnormality, staining re-agents showing the usual forms to be present; none are pigmented.

Jan. 6th, 1894.	R.B.C.	=	3,460,000
	W.B.C.	=	10,000

The red show the same variation in size and a tendency sometimes to curl up. There is no definite poikilocytosis (though a few show a slightly oval form.)

Jan. 17th, /

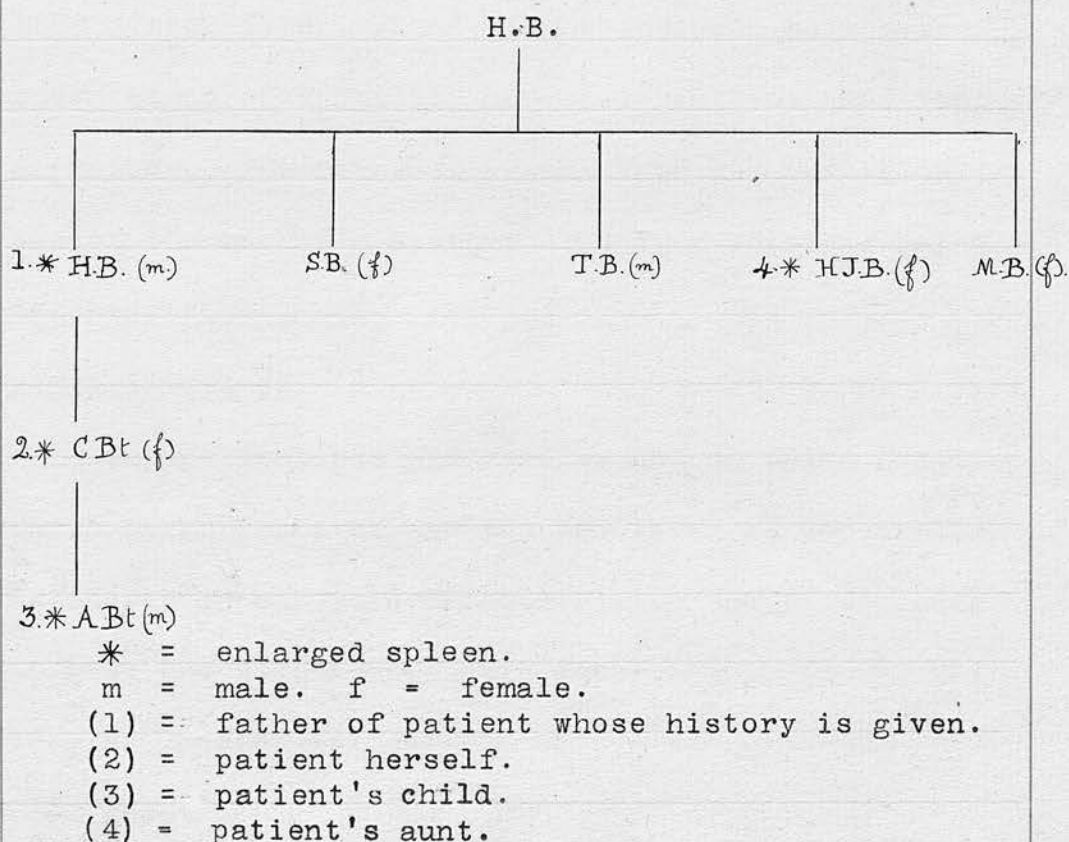
Jan.17th, R.B.C. = 3,100,000
 W.B.C. = 15,000
 Haemoglobin = 30 p.c.

The patient has just menstruated.

Feb.1st, R.B.C. = 3,220,000
 W.B.C. = 10,000
 Haemoglobin = 50 p.c.

The patient is now feeling much better; the tenderness over the spleen has very much decreased.

Table Showing Hereditary Condition.



CASE V.

(From personal observation.)

Severe anaemia. Irregular temperature.Dark coloured urine. Vomiting.Enlargement of spleen but no gland change.

Alice H., age $13\frac{1}{2}$. Admitted to Guy's Hospital,
Sept. 13th, 1892.

Family History.

The patient's father and mother are quite well.
There were eight children, of whom five are living.
The patient is the only girl. The other four are
quite healthy. Three died quite young. There were
four miscarriages. None of the children have ever
shown signs of syphilis, nor suffered from snuffles
or rashes. The maternal grandmother was phthisical;
one of the mother's sisters died from a "tumour below
the heart".

Previous Illnesses.

The patient has had measles and whooping cough.
Since seven years of age she has lived at Southall,
but never in any malarial district. She is supposed
to have had slight rheumatic fever.

History of Present Illness.

About /

About four years ago, she complained of pain in the left side, which was somewhat paroxysmal in character, and has troubled her at intervals ever since. About the same time as this pain began, a swelling was noticed in the left side, and has increased ever since; about three years previous to admission, she became very pale and weak, perspiring very severely at night. She has had no cough, nor, till the present time (Sept. 1892), has she suffered from haematemesis, haemoptysis or epistaxis. No enlarged glands have ever been noticed.

Present Condition.

Patient looks pale, and anaemic, and there is a slight yellow tinge of the skin; the conjunctivae are clear; (there are many freckles on the face, which at first might mask the real colour). The lips and tongue are pale. There are no enlarged follicles at the base of the tongue; the tongue is slightly furred, the right tonsil is slightly enlarged, the left not so. There are no enlarged glands in the neck, nor is the thyroid enlarged. The salivary glands are normal. None of the glands in the axillae, groins, etc., appear enlarged.

The /

The respiratory system appears to be normal.

Circulatory system. The precordial dulness is normal. The cardiac impulse is in the left fifth space internal to the nipple line. At the apex, there is a blowing systolic murmur which is lost on following to the axilla, and is then replaced by the 1st sound. In the pulmonary area, there is also a soft haemic systolic murmur. At the 2nd right costal cartilage the sounds are normal. There is a slight venous hum.

Examination of Abdomen. The liver dulness begins at the lower border of the 5th rib and does not quite extend to the costal margin, so that there is no hepatic enlargement. There is a large resisting, moveable, hard, non-fluctuating, painless tumour, slightly rough on the surface, projecting downwards and forwards from under the left costal margin, it being possible to pass the fingers between it and the costal margin. Over this swelling, the note is uniformly dull; the right limit is half inch to right of the umbilicus, the lower 1 inch above the level of the iliac crest; the lower margin is distinctly notched, so that the tumour is evidently spleen /

spleen.

Urine. Dark coloured, Spec. Grav. = 1014.
React. acid, no albumen, blood, sugar or bile.

Eyes. Ophthalmoscopic examination, negative.

Blood. R.B.C. = 2,700,000; W.B.C. = 10,000.

Temp. Vide chart.

Progress of Case.

Oct. 4th. 1892. R.B.C. = 2,600,000; W.B.C. = 10,000;
Haemoglobin 35 per cent.

" 5th Motions very relaxed.

" 7th A small gland (?) felt at the margin
of the right sterno-mastoid.

" 8th Slight epistaxis. The patient shows
a slight yellow tinge.

" 9th Urine orange coloured, acid, but no
albumen, blood, sugar or bile.

" 13th The anaemia is becoming more marked.

" 17th R.B.C. = 2,400,000; Haemoglobin
30 per cent.

Nov. 6th The patient is troubled with severe
vomiting, and great pain in the left
side; here a distinct rub can be felt
and friction heard; the spleen has
become enlarged and is tender on
palpation.

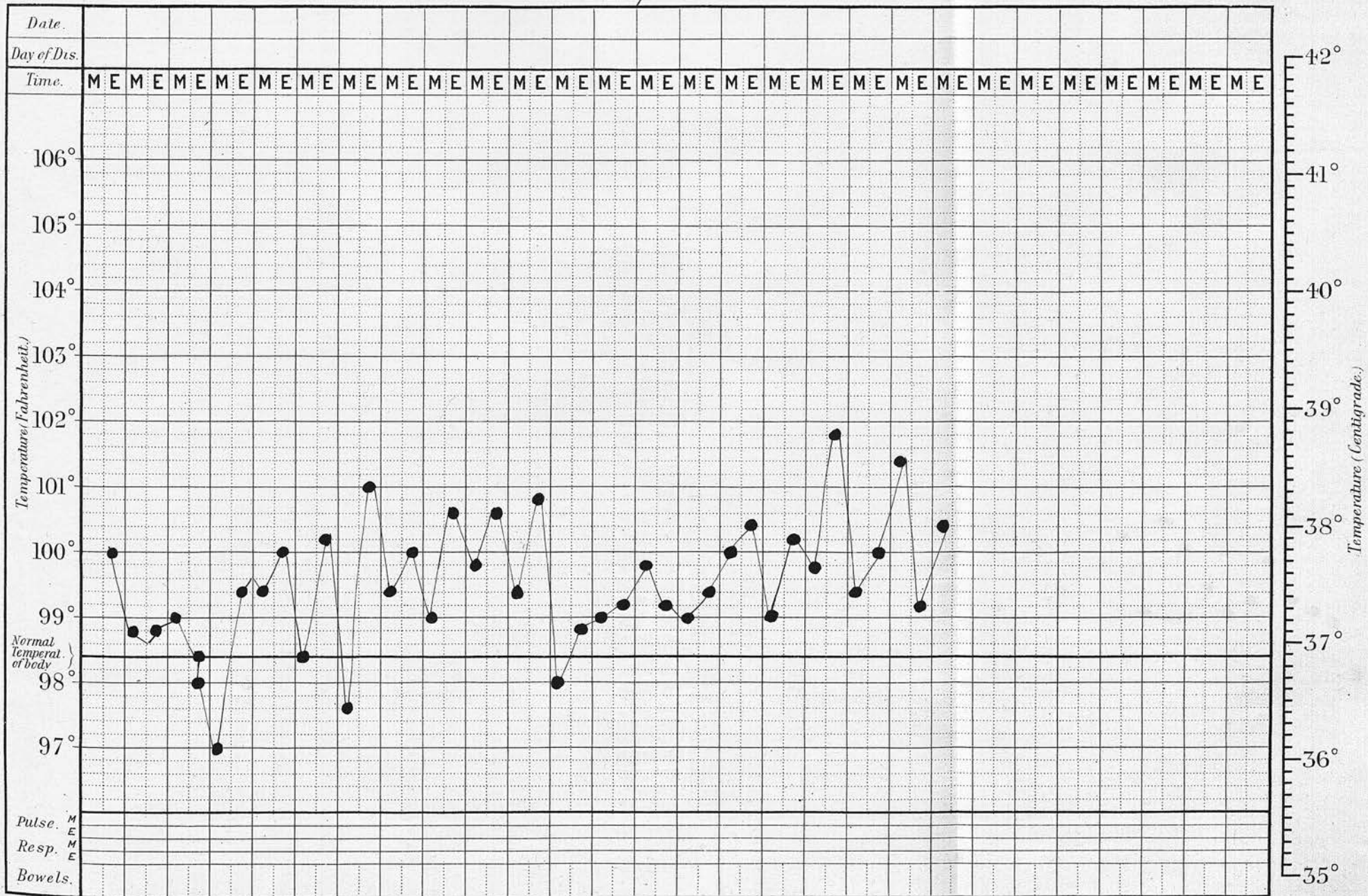
" 11th R.B.C. = 1,370,000; W.B.C. normal;
Haemoglobin 28 per cent.

The urine still continues dark coloured, the
average amount = 25 oz. and the average of urea =
grs 160 per diem.

The patient continued in this condition till taken
home by her parents. She died in February 1893, but
no post mortem was made.

In /

Name *Alice H* Age *13½* Disease *Splenic Anaemia* Admitted *to follow p 205*



In this case, no special examination for pathological pigments in the urine was made, but the colour is highly suggestive of pathological urobilin¹ .

1. I am indebted to the kindness of Dr. Frederick Taylor for the opportunity of seeing this case.

CASE VI.

(From personal observation).

Enlarged Spleen and Liver.Pigmentation of Skin.Anaemia.Irregular Temperature.Exophthalmos and Goitre.

Martha S., age 25, Domestic Servant.

Family History.

The patient's father is alive and enjoys good health except for occasional attacks of 'rheumatic gout'; her mother died when she was two years old; the cause of death is unknown to the patient.

There are six other children, two brothers and three sisters older, one sister younger than the patient. All are perfectly strong and well, and so far as is known, none have ever complained of 'swelling in the side'.

Previous History.

The patient says that up to May, 1893, she had always enjoyed good health; at that time she suffered from 'anaemia' and found it difficult to do her work. This got somewhat better with change of air to the seaside. She has not, so far as she knows, had any of the usual illnesses of childhood.

Surroundings /

Surroundings and habits. The patient has always lived in the Midlands and has never been out of England, nor lived in any malarial district. She has always had a comfortable home, and her work has never been severe. There is no alcoholic habit.

Present Illness.

This began about September, 1893, so far as the patient is aware, the first thing noticed being that she could not fasten her clothes and that she began to lose flesh. This continued till her admission into hospital, November 1893.

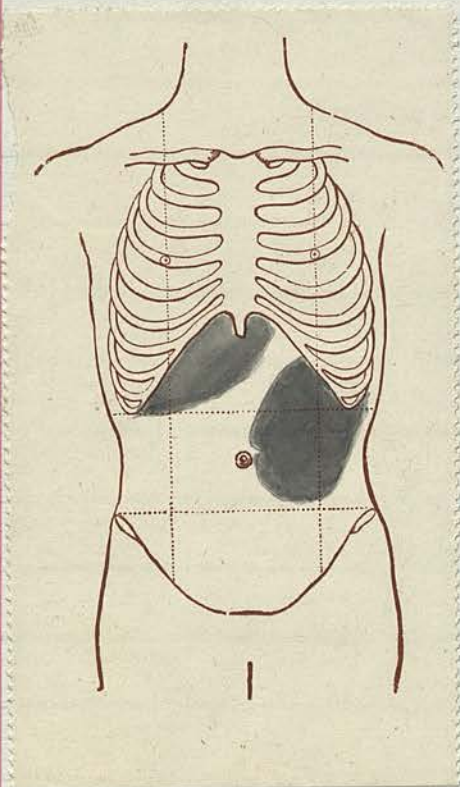
Present Condition.

The patient is a well-developed girl, of a very dark complexion, the skin of the forehead being quite olive, and in the flexures is especially dark, showing actual pigmentation, while scattered over the fore-arms and neck are small, darkly pigmented patches similar to those already described in Case III., q.v. There is some exophthalmos, and a well-marked goitre which shows some pulsation. The lips are a good colour but the conjunctiva far back shows an anaemic appearance, though at the margins, it is fairly red.

The /

The teeth are good and regular, the tongue is smooth, red, not pigmented. The appetite is good, so is digestion, the patient not being troubled with pain or discomfort as regards this function. The bowels are fairly regular.

Physical examination of the abdomen shows that the liver is enlarged, projecting downwards to a level



of three-and-a half inches above the umbilicus; but does not present any other abnormal feature. The spleen is also found to be greatly enlarged, reaching to the umbilicus downwards and inwards, and to the level of the crista ilii downwards in the flank. There is a distinct notch exactly opposite the

umbilicus. The surface is smooth, regular, and palpation is painless.

Examination of the abdomen is otherwise negative; there is no evidence of fluid. Examination of the circulatory system shows some cardiac dilatation with soft, /

soft, blowing murmurs at the base and apex. Pulse = 120, soft, rapid. There is considerable pulsation in the vessels of the neck and in the goitre as mentioned. The respiratory system is negative on examination.

Nervous System.

The patient sleeps badly and cries a good deal, but does not suffer from any abnormal subjective sensations; and is not hysterical.

Physical examination does not show any abnormality in sensation or motion. Reflex condition normal.

Urinary System.

Urine in 24 hours	= 820 to 1050 cc.
Colour	very dark amber with red tinge.
Reaction	acid, sometimes neutral.
Spec. Gravity	1020 - 1025.
Urea	12.5 - 20.5 grms.
Albumen	faint trace.
Blood	No reaction.
Bile	" "
Sugar	" "
Phosphoric acid	1.3 grm.
Sulphuric acid	1 grm. (approx).
Indol	No reaction.
Skatol	" "
Peptone	" "

Spectroscopic examination showed the presence of pathological urobilin. It will be noticed that many of the estimations show figures under the average, but the amount of urine passed in the twenty-four hours was /

was always small.

Blood: Date of examination 19/XII/93.

R.B.C. = 3,370,000.

W.B.C. = 10,000.

Haemoglobin = 35 per cent.

The red discs are somewhat variable in size, and there is some poikilocytosis but no nucleated forms are seen.

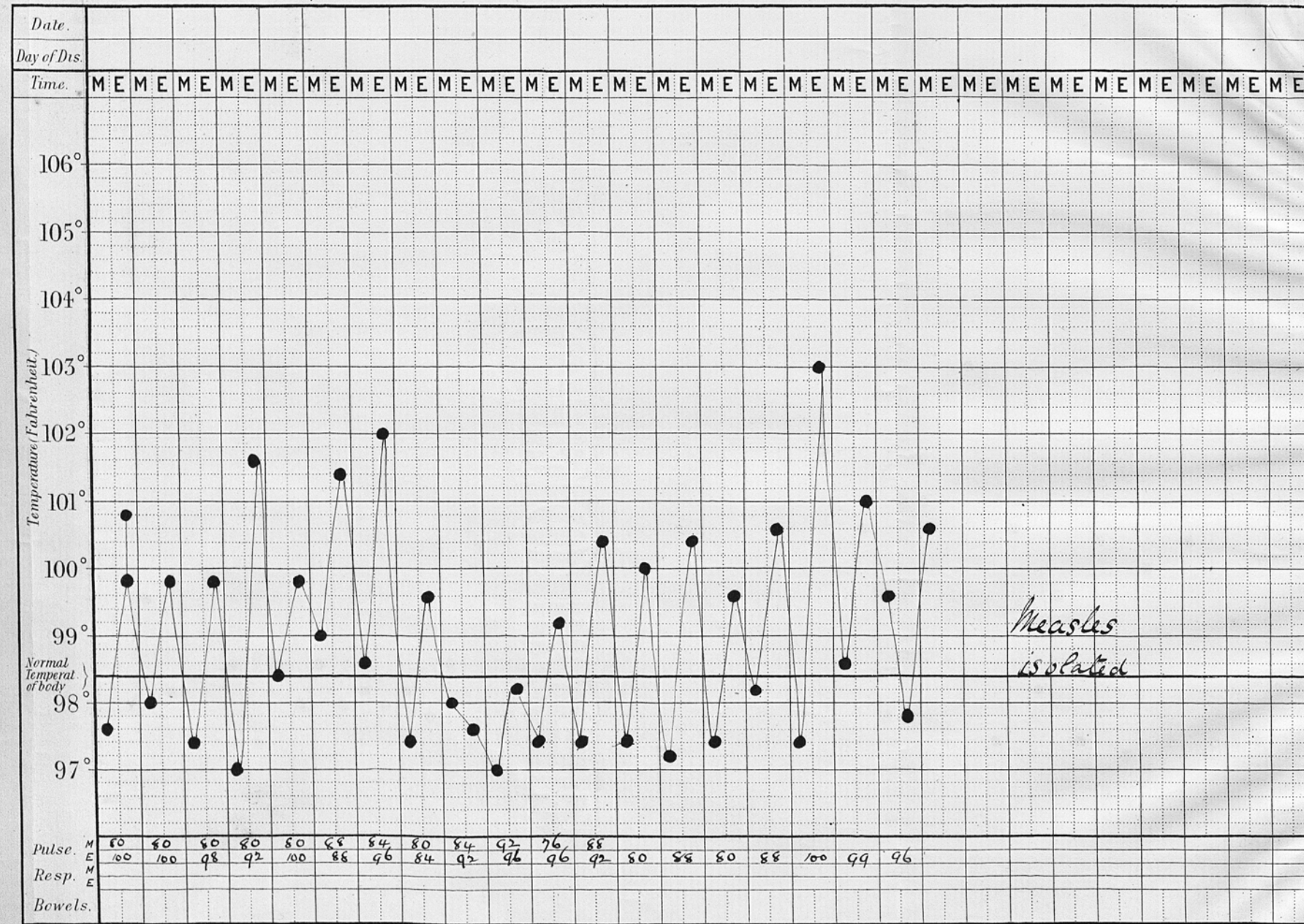
The white cells show only normal forms.

The temperature varies greatly, being generally elevated in the evening, showing at times a very considerable rise.

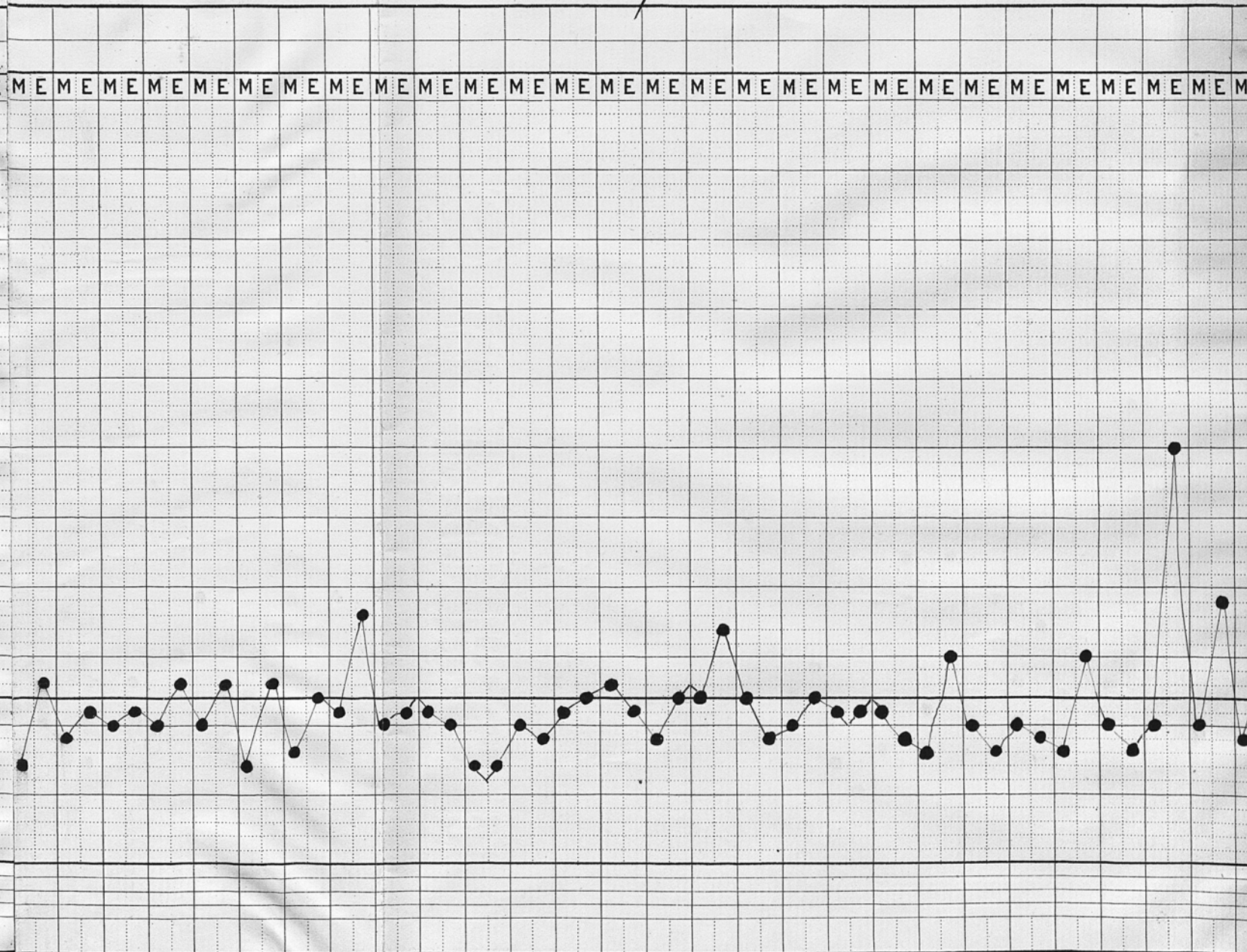
Prognosis of the case.

There was some improvement in the patient's general condition, especially in the exophthalmos and goitre. While in hospital, the patient contracted measles, and when this subsided, the curious fact was observed that the temperature, which before had been very irregular, became very much steadier for some time, rarely rising above 99° in the evening, often being subnormal, vide charts p . The pigmentation appeared to increase to some extent and there were attacks of epistaxis. The patient remains in this condition. (March 1894).

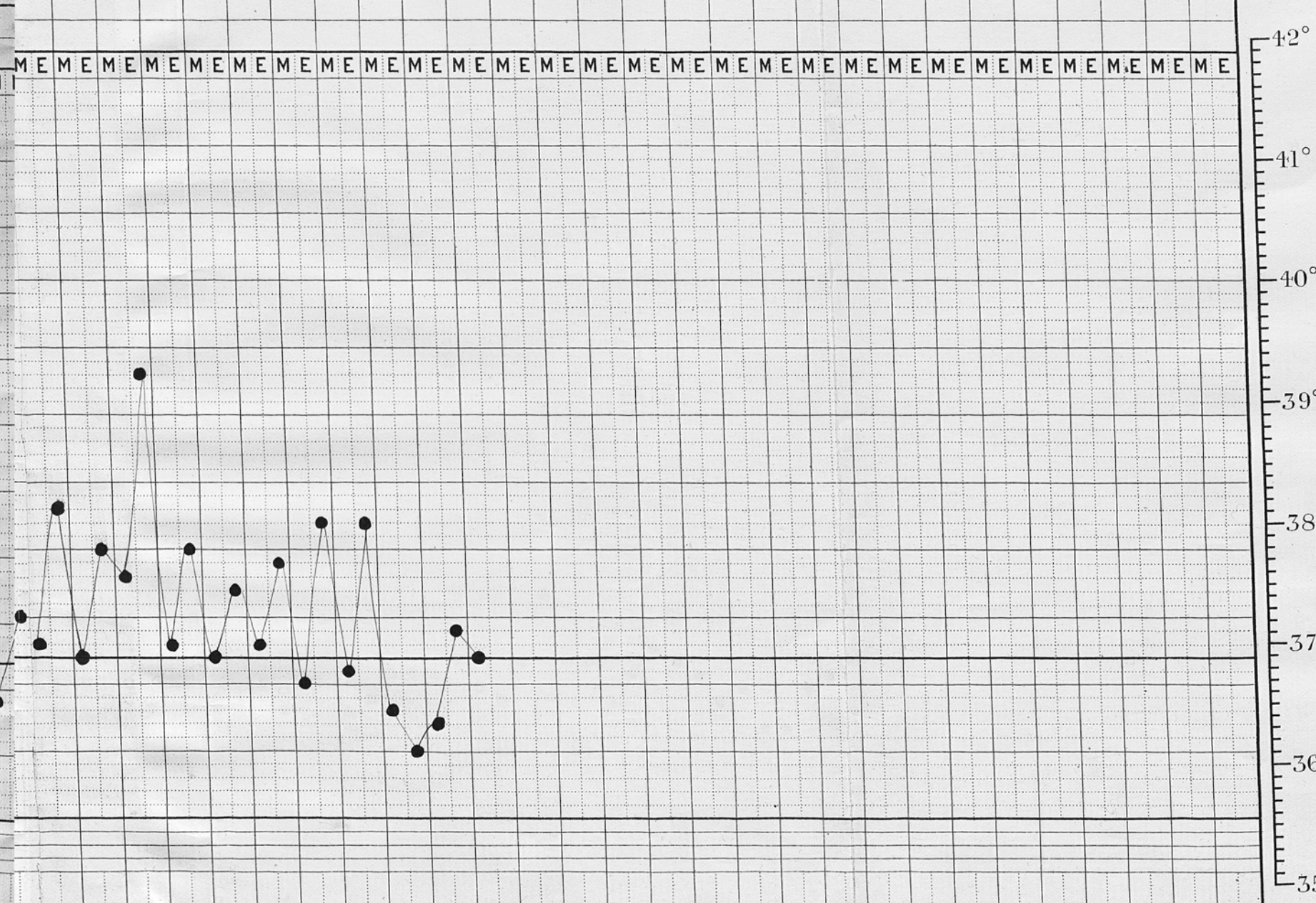
Name *Martha S* Age _____ Disease _____ Admitted _____



Age _____ Disease *Splenic Haemia* Admitted _____



Age _____ Disease _____ Admitted _____



CASE VII.

(From personal observation).

Hereditary History of Enlarged Spleen.Enlarged Liver.Febrile Attacks.Decrease of R.B.C.No increase of W.B.C.

A.P., jun., age 38. Married.

Family History.

His father enjoyed good health till seventy, when he became diabetic (gouty). His mother, born 1825, died 1888, suffered from enlarged spleen (vide Case XI).

Previous History.

The patient was born two years after his mother was known to have an enlarged spleen. He lived in London till 5, and then at Wimbledon till 11, and has never lived in any malarial district. He was a somewhat dark-skinned baby and this became more marked when he was about five years old. He became somewhat deaf when about eight. When about four he was seen by Sir Wm Gull, who considered he had 'ague-cake'. In about the year 1875 he had some illness, and after this /

this he was subject to fits of epistaxis and fainting. These have varied in severity up to the present date. He is also liable to 'bilious attacks'. These "begin with a feeling of chilliness, slight shivering and general uneasiness, soon followed by great pain in the muscles of the limbs and thorax, greatly aggravated by movement. At no stage is there any sensation of heat. There is decided icterus; the pulse is rapid and the temperature 101° or 102° F.; the skin is moist but seldom profusely perspiring and the tongue is usually clean. The spleen, always large, becomes somewhat increased in bulk and very tender. The same observation applies to the liver, but here the tenderness is not so marked. The attack lasts from three to five days and gradually subsides. Between the attacks, he feels pretty well, though he frequently has some aching in the left side" §. During an attack of this kind he passes urine of a very dark red-yellow colour.

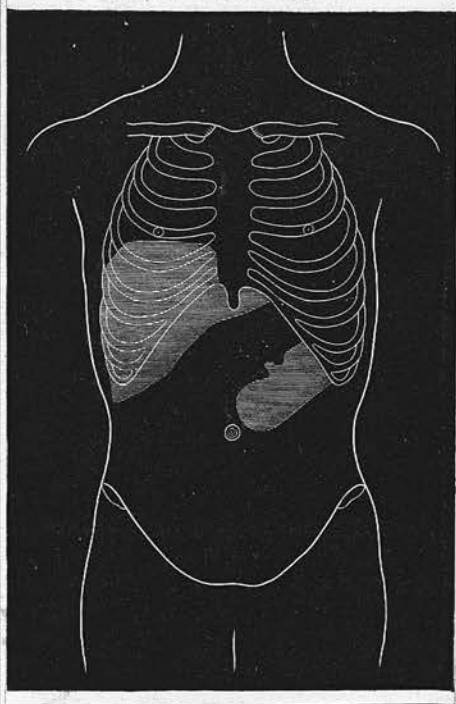
Present Condition.

(Nov. 1892). The patient is a well developed man
(wt /

§ Dr Wilson, Clin. Soc. Trans. vol. XXIII.

(w^t = 10st.) his complexion being very dark and sal-
low. There is well-marked anaemia, especially of the
mucous membranes but no anasarca. Examination of the
circulatory system is negative, while that of the
respiratory system shows evidence of a recent attack
of pleurisy in right side. The liver is enlarged,
the upper border being in the fourth right space, the
lower projecting an inch below the costal margin. On

FIG. 3. (Mr. A. P., jun.)



palpation it is smooth and
firm but not hard. There is
also considerable enlargement
of the spleen which projects
beyond the costal margin
downwards and towards the
umbilicus for about four
inches. On palpation two
notches are felt and the
organ has a firm but round-
ed border, feels very hard,

and a resistant boss can be felt near the margin bet-
ween the notches. No enlarged lymph glands can be
found. The urine at present is negative, but there
have been periods of albuminuria, but no blood nor
casts /

casts found. Urea = 340 grains per diem average.

There is considerable deafness, otherwise physical examination is negative.

Blood: Oct. 1892 .

R.B.C. = 3,820,000

W.B.C. = 12,000

Haemoglobin = 50 per cent.

Previous examination in March gave as a result:

R.B.C. = 3,300,000

W.B.C. = 16,000

Haemoglobin = 60 per cent.

The red corpuscles were all good average size; no nucleated ones were found and there was no poikilocytosis. The white corpuscles were of the usual forms, no abnormal forms being found.

A marked feature in this case was the passage of highly coloured urine during a febrile attack. Examination by the spectroscope showed that this was due to a large amount of pathological urobilin.

The patient is still alive (1894) but is losing ground.

CASE VIII.

(From personal observation.)

Hereditary history of Anaemia, Asthenia and Enlargement of Spleen.

Reduction in number of R.B.C.

Alice P., age 10.

Family History.

Patient is the second child of A.P. (Case VII). q.v.

Previous History.

Negative.

Present Condition.

She is a well developed and well nourished girl and very active.

She is distinctly sallow but not strikingly anaemic, though careful examination of the nails and eyelids reveals a paler tint than is natural. Physical examination of the heart and lungs is negative. Renal system negative also. Examination of the abdomen shows that the spleen projects below the ribs for $2\frac{1}{2}$ inches. The liver dulness does not seem increased. She has no marked splenic symptoms, except that at times she complains of a pain in her left side which always means, her mother says, that "she will be out of sorts for /

for a few days". No enlargement of lymph glands to be discovered.

Examination of the blood (Oct. 1892)

R.B.C. = 3,800,000

W.B.C. = 20,000

Haemoglobin = 60 per cent.

R.B.C. present no deformities. W.B.C. no abnormal forms.

CASE IX.

(From personal observation).

Hereditary history of anaemia.Enlarged spleen; febrile attacks, and yellow coloration.Reduced number of R.B.C.

N.T., (male), born 1880.

Family History.

Patient is the second child of Mrs T. (Case XII).

Since the age of three months he has had a sallow complexion and is not strong; he is very susceptible to cold and often gets feverish. The yellow tinge becomes much worse on exposure to cold as in taking a cold bath.

In 1890 the spleen was found to project $2\frac{1}{2}$ inches below the costal margin. At present (January 1893) it projects $3\frac{3}{4}$ inches, although the febrile attacks have not been so frequent, (patient has been taking iron and arsenic). The liver is not enlarged. There are no enlarged lymph glands. During a febrile attack, the spleen becomes larger, but is not particularly tender on palpation; the urine is, under the same conditions, of a dark amber colour, but does not show any albumen.

Blood :	R.B.C.	=	3,150,000
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	W.B.C.	=	5,000.
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The R.B.C. are average size, and no abnormal forms, either red or white, are seen.

CASE X.

(From personal observation).

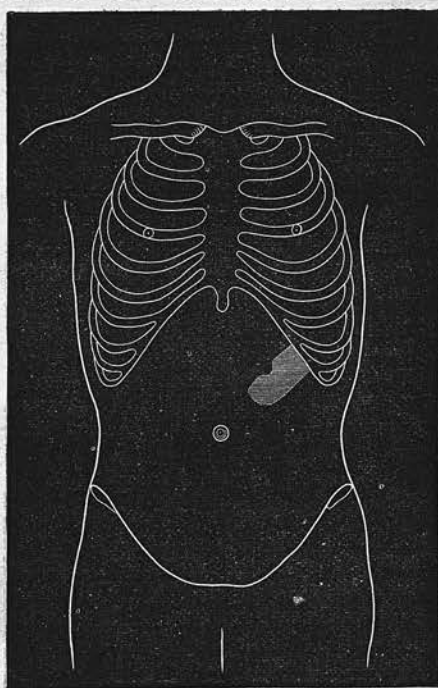
R.T., (male), born 1881.

Family History.

Patient is the third child of Mrs T. (Case XII) and younger brother of N.T. (Case IX).

At about three months old he also became sallow, and as he grew older he always remained, to a certain extent, delicate. He shows the same susceptibility to cold as his elder brother, and suffers from the same febrile attacks.

In 1893 the spleen is found to project nearly four inches below the costal margin. There is no apparent enlargement of the liver.



CASE XI.

(Recorded by Dr. Wilson). (16).

Family history (vide table II. p.225)Enlarged spleen; jaundice.Progressive asthenia and anaemia.Death.

Mrs A.P., born 1825, died 1888.

Family History.

Father died aged 88; mother died at 48, with liver trouble and dropsy.

Two sisters give negative histories. One brother 'suffered from his liver', died 1876. None of these are said to have had sallow complexions.

Previous History.

Health was said to be very good, the patient being brought up mainly in Brixton and Kensington. After her marriage (at 25) she lived in London, then at Wimbledon, Torquay and Tunbridge Wells. In 1851, shortly before the birth of her first child, she had an attack of jaundice after which she was always more or less sallow. In 1858 she was seen by Sir Wm. Gull, who considered that she, as well as her two eldest children, had become infected with ague as all three had enlarged spleens.

The /

The patient's health remained about the same till 1884, when she began to fail, the spleen becoming larger, the liver also showing some increase in size. The anaemia became more marked and the icteric tinge more pronounced.

The blood was examined in the latter part of 1887 but not numerically. There was no leucocytosis "and in shape, size and behaviour, the red and white corpuscles were normal".

The patient died in 1888, "after a gradual and steady failure of vitality", the condition suggesting "some malignant" disease.

CASE XII. (Recorded by Wilson and Stanley (16).

Hereditary History of Enlarged Spleen.

Jaundice.

Anaemia.

Asthenia.

Death.

Autopsy.

Mrs T. Born 1851. Married 1887. Died 1891.

Family History.

Father as in Case VII. Mother subject of splenic anaemia, Case described above, No.XI. Brother similarly affected, Case VII.

Previous History.

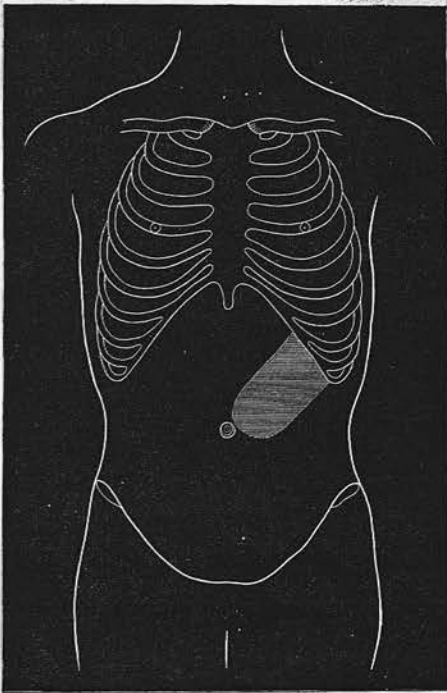
The patient became sallow when five or six years old, and when about seven was seen by Sir Wm Gull, who found enlargement of the spleen (vide Case VII). Up to about 1870 she enjoyed fairly good health, but after this date she suffered from what seems to have been biliary colic, and on one occasion she passed a gallstone. She has not had attacks with elevation of temperature to the same extent as her brother (A.P., Case VII). The patient has had four children, two of whom have a sallow complexion and enlarged spleen (vide /

(vide supra Cases IX and X). She has had subsequently to the birth of her youngest child (in 1884) two miscarriages and a still-born child.

Present Condition.

(1890). The patient is rather stout, her complexion is somewhat sallow, and her eyes have a slight

FIG. 1. (Mrs. T.)



icteric tinge. At times when otherwise perfectly well, there is 'well-marked jaundice'. The spleen is greatly enlarged, the liver is somewhat enlarged.

There is nothing abnormal found on examination of the other systems.

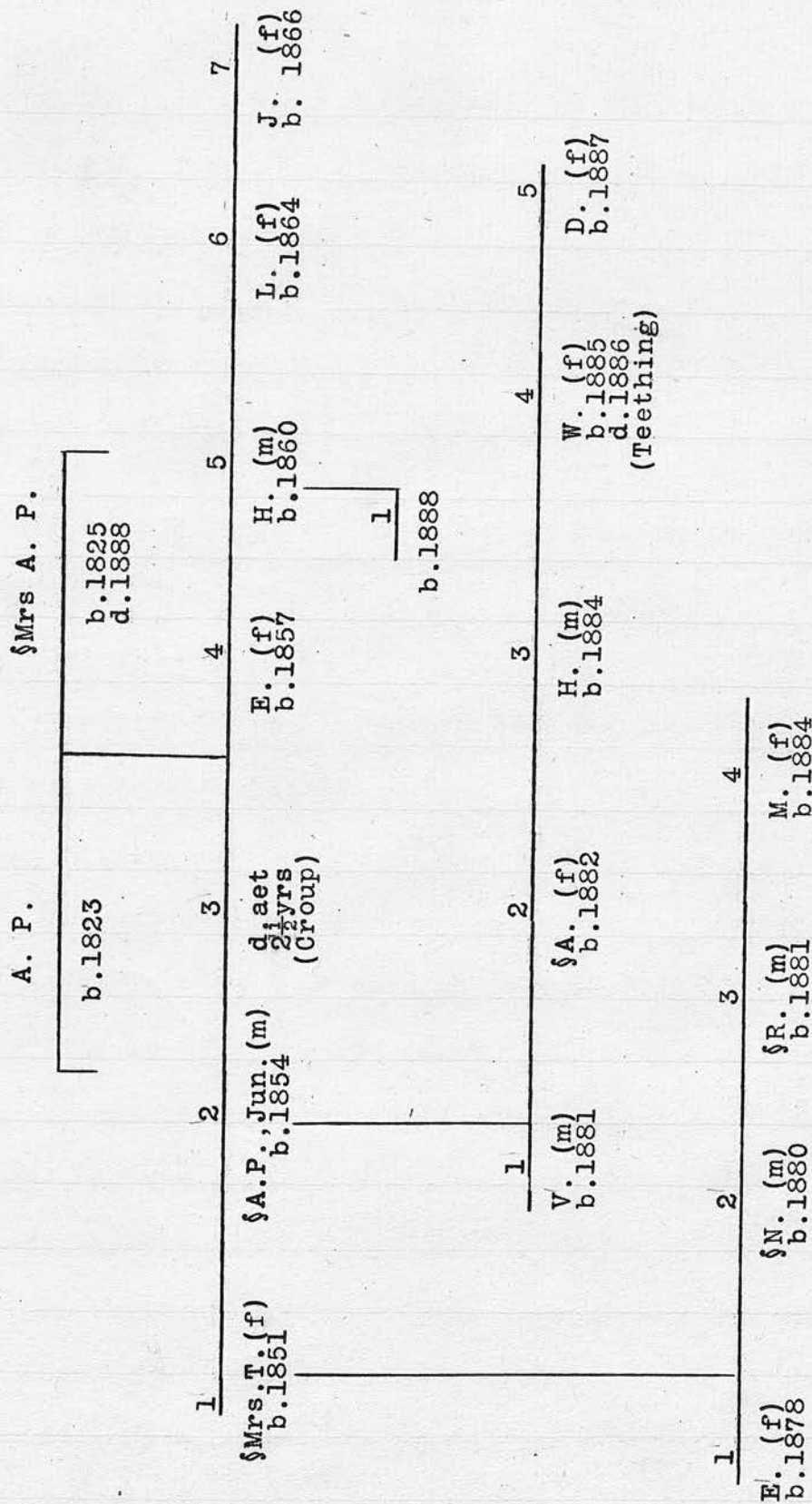
There is no enlargement of any of the lymphatic glands.

Subsequent History.

The patient became pregnant in 1890, and as she approached term her health began to fail in a marked manner; she slept badly, became very short of breath on slight exertion, and at the end of February 1891, developed decided 'jaundice' with nausea, retching, vomiting and complete anorexia. She was confined to her /

her room, and gradually became so weak and feeble, that she could hardly walk unaided from the bed to a chair. She became extremely anaemic but not emaciated, vide Wilson and Stanley (16).

Patient died 28th March. (For post mortem report (vide p. 70).



Cases marked (§) show Enlarged Spleen and Sallow Complexion.

CASE XIII.

(Recorded by Williamson 17).

Epistaxis. Weakness. Enlargement of spleen. Nopalpable lymph glands.Reduction of R.B.C.. and haemoglobin.Irregular temperature.Death. Autopsy.

Robert P., age 9. Admitted to Manchester Royal
Infirmary, Feb.15th, 1892.

Family History.

The patient has three brothers and two sisters,
all of whom are healthy.

Previous History.

The patient has been very pale for two years; and
for twelve months, has been subject to attacks of
epistaxis about every two weeks. Two months ago the
face became puffy, the abdomen was noticed to be en-
larged and the patient began to be troubled with short-
ness of breath.

There is no history of any special illness. He
was born in Liverpool and has lived there and in Man-
chester. He has never had ague, nor been exposed to
malarial infection. His surroundings and habits have
always been good.

State on admission.

The /

The patient is very anaemic; the face is puffy, but there is no oedema of any part of the body. He is fairly well nourished. There are no purpuric spots to be seen. There are no signs of congenital syphilis; no signs of rickets. There are no enlarged glands in the neck, axilla, or groin. The tonsils are not enlarged.

The abdomen is much enlarged, but there is no ascites. The spleen is greatly enlarged. The splenic dulness begins at the seventh rib in the axillary line. The spleen can be felt below the ribs, reaching down beyond the umbilicus to the level of the iliac crest. The liver dulness begins at the sixth rib, and the edge of the liver can be felt below the ribs, extending mid-way between the costal border and the umbilicus.

There is no palpitation, nor dyspnoea, Pulse 80, regular, of low tension. Pulse tracing shows a good dicrotic wave. The cardiac impulse can be felt in the fourth left intercostal space in the nipple line. There is no increase in the cardiac dulness. A loud rough systolic murmur is heard at the apex; it is also heard, but less distinctly, at the base and at the tricuspid region, but is not conducted to the back /

back. There are no changes in the lungs. The nervous system is normal.

Ophthalmoscopic examination - Fundi normal.

Urine S.G. 1010, alkaline, no albumen, but excess of phosphates.

Blood:-	R.B.C.	=	3,030,000 per cmm.
	W.B.C.	=	4,000
	Haemoglobin	=	22 per cent.

The patient was discharged but re-admitted a month later, and during this interval he suffered severely from epistaxis. On re-admission, he appears much more anaemic.

June 1st. - R.B.C. = 2,510,000

W.B.C. = 2,000

June 29th. - The spleen has increased in size and now reaches down to the pubes and extends slightly across the middle line. Liver not larger than before.

R.B.C. = 2,700,000

W.B.C. = 7,500.

July 8th. - Face puffy. Slight oedema of the dorsal surfaces of feet.

Blood very watery, and shows a considerable number of poikilocytes, also a few large and a few small red /

red corpuscles. By special staining methods, no increase of the eosinophilous cells was found, nor any other abnormal form; the only change noticed in the leucocytes was a slightly greater proportion of small mononuclear white corpuscles (lymphocytes?) than in healthy blood.

The urine was dark in colour, acid, S.G. = 1010, no albumen, no peptones nor sugar.

July 14th. - Patient much worse, very drowsy, face covered with perspiration, urine very dark, almost porter-coloured, no bile present, no deposit, S.G. = 1020, acid, faint trace of albumen. There is occasional retching, and severe pain in the abdomen.

Death.

Name *Robert P*

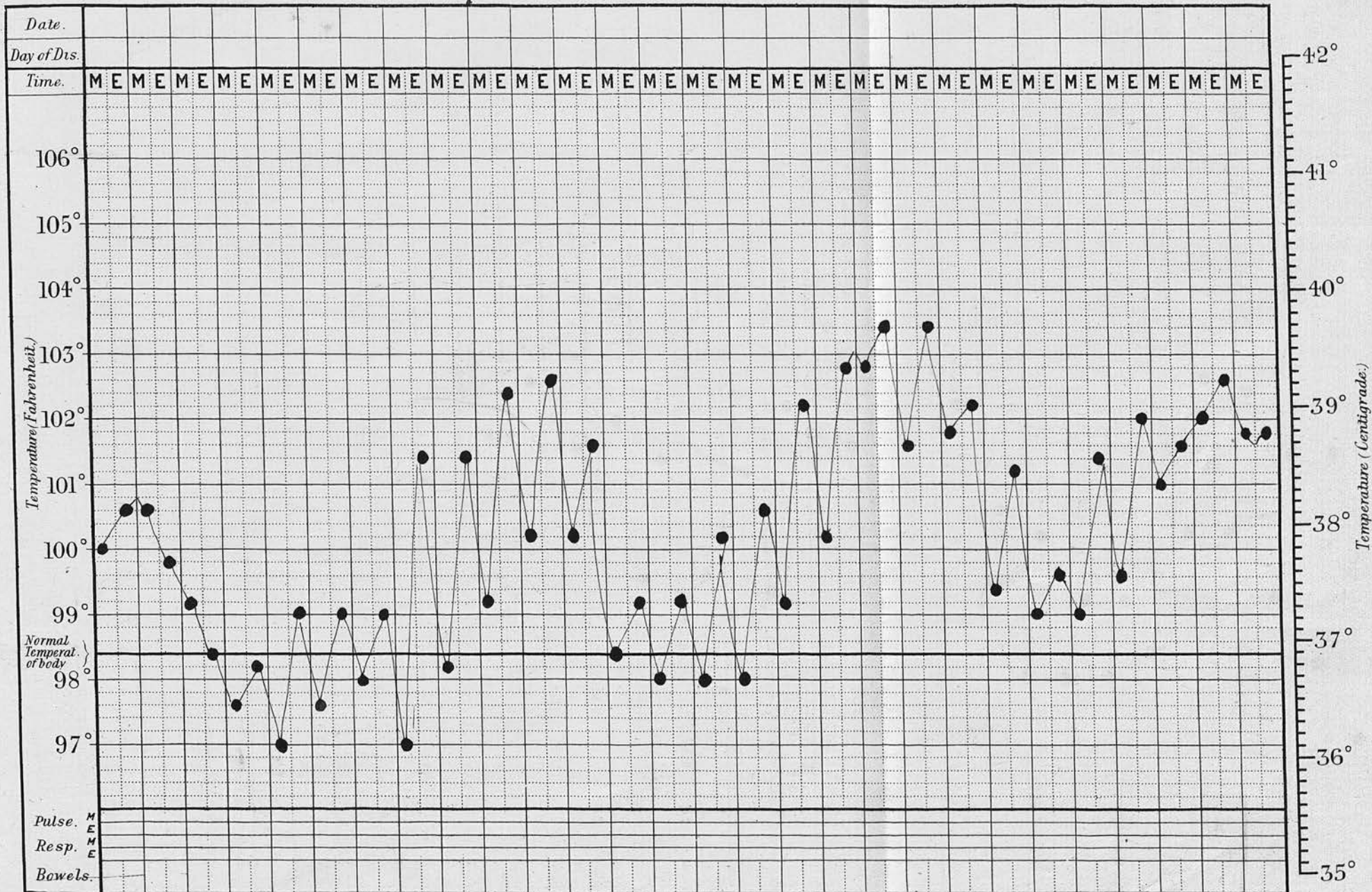
Age *9*

Disease

Splenic Anaemia

Admitted

to follow p. 228



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A VERTICAL LINE MAY BE DRAWN AT THE END OF EACH WEEK OF DISEASE.

FOR NOTES OF CASE SEE BACK OF CHART.

Printed & Published by H.K. Lewis, 136, Gower Street, W.C.

(RIGDEN'S CLINICAL CHART.)

CASE XIV.

(Recorded by Williamson 17).

Weakness. Haematemesis. Epistaxis. Nausea.Irregular temperature. Enlargement of spleen.Reduction of R.B.C.

James F., age 21. Admitted to the Manchester
Royal Infirmary, 4th June, 1890.

Previous History.

Previous health good until about a year and nine months before admission. At that date he suffered from general weakness, indigestion and vomiting of blood. He was a soldier at the time, and was stationed at Jersey. For nine months he was a patient at the military hospital there on account of the above mentioned symptoms. He then returned home and was confined to bed for three months. At this time there was oedema of the legs. He gradually improved and for nine months he has been able to walk out. The haematemesis occurred at intervals until six months before admission. On six or seven occasions he has passed blood in his motions. He has suffered from epistaxis twenty or thirty times during the last twelve months, and frequently there has been bleeding from /

from the gums in the morning. There is no history of syphilis, gonorrhoea or alcoholism. Three years ago whilst in Jersey, he had an attack of shivering. This was followed by two similar attacks; but in about three days he was quite well. He continued well for twelve months until the onset of the dyspeptic symptoms and haematemesis above mentioned. There is no history of malaria. Patient has never lived in any malarial district, nor in any tropical country. There is no history of any other illness. Nothing of importance is found in the family history.

Present State.

The patient is a thin anaemic man. He complains of weakness and shortness of breath. Temp. 99.4. In the left groin there is an inflamed lymphatic gland about the size of a walnut. There is a slightly enlarged gland in the right groin. Other lymphatic glands not affected. The abdomen is enlarged. No ascites. Liver dulness normal. Spleen greatly enlarged, the dulness beginning at the sixth rib in the axillary line. The spleen is felt below the ribs extending down to about the level of the umbilicus.

Examination /

Examination of the blood showed a diminution of red blood corpuscles; only 3,270,000 red corpuscles were present in one cubic millimeter. There was no excess of white corpuscles and the haemoglobin was reduced to 20 per cent. The apex of the heart was pushed upwards into the fourth intercostal space and was felt just below the nipple. A systolic murmur was heard over the pulmonary area. Lungs normal. Urine S.G. 1030, acid, no albumen, no sugar. Ophthalmoscopic examination - vessels of left fundus very tortuous. No retinal haemorrhages or other changes in either fundus.

July 9th, 1890. - R.B.C. = 2,560,000. No increase of the W.B.C. Patient troubled with nausea, severe pain in the splenic region, night sweats, and evening rise of temperature.

CASE XV.

(Recorded by Dr Saundby 19)

Hereditary history of enlarged spleen with passage of dark coloured urine.

Great anaemia; intermittent attacks of illness with increase in the size of the spleen.

Pathological pigments in urine.

W.H.E., age 16, came under treatment for cough and pain in the left side, the duration being two days. Pulse 120, respiration 18, temp. 102°. Percussion showed considerable diminution of resonance posteriorly at the left base; breath sounds harsh; inspiration prolonged. The cardiac apex was found in the fourth left interspace $3\frac{1}{4}$ inches to the left of the middle line. There was a systolic murmur at the base, propagated into the neck, and a loud bruit de diable in the jugulars. In the left hypochondrium there was a large tumour, which reached across to beyond the middle line of the abdomen, the right border of which was rounded, tense and presented a well-defined notch. There was much tenderness on palpation. No enlargement of the liver was detected. There was constipation and extreme difficulty in micturition; the urine was porter-coloured and deposited brown flocculent /

flocculent matter, which was composed of urates, oxalates, bloodcasts and material resembling broken-down bloodcasts. S.G. = 1017. Albumen was present, but no sugar or bile. Spectroscopical examination (by Dr. MacMunn) showed the presence of methaemoglobin and pathological urobilin.

The patient's skin was of a dusky yellow. There was a history of the patient's having always passed dark urine from his birth; that the enlargement of the spleen had been known to exist for some years; that his father died at the age of thirty-seven with the same symptoms of enlargement of the spleen (which weighed $7\frac{1}{2}$ lbs. at the post mortem) dusky skin and dark urine, and that the younger of two other living children, both girls, passed the same peculiar coloured urine, though otherwise well. This attack passed off in a few days, the spleen becoming smaller.

Examination of the urine on another occasion, but not during an attack, showed the presence of indican, urobilin, uroerythrin and haematoporphyrin.

Vide table p.237, relating to this case and the next.

CASE XVI.

(Recorded by Dr.Saundby 19).

Hereditary history of enlarged spleen with passage of dark coloured urine.

Great anaemia; no glandular enlargement; no increase of white blood corpuscles.

Pathological urobilin, etc., in urine.

Death from asthenia.

Post mortem. Enlargement and pigmentation of the spleen; atrophy of suprarenals.

B.E., age 18, became anaemic two years ago, and gradually weaker, with loss of appetite.

Present Condition.

The patient has a dark, dusky complexion, and suffers severely from weakness, sickness, and loss of appetite. Physical examination shows increase of cardiac dulness with systolic murmurs at the base. There is considerable enlargement of the spleen which reaches nearly to the umbilicus. The urine was of a deep brownish-yellow colour, reaction acid, specific gravity 1012; no albumen; no blue colour with guiacum and ozonic ether. With nitric acid, it gives only violet and red. The colour is due to urobilin indican, and it also yielded onucholin. It contained no blood pigment or bile pigment (Dr MacMunn). Examination of the blood /

blood showed no increase in the leucocytes, and the red cells appeared very pale. They were not enumerated however.

A year later, the patient got over-fatigued and felt faint, and became rapidly worse, with severe fainting fits, sickness, headache and epigastric pain. Temperature 102; the tongue was pale and clean; the spleen reached to the umbilicus; the urine was dark. The patient died comatose on the fourth day after being taken ill.

Report of post mortem examination. Body well developed; rigor well marked; the skin of face and hands was dark; there was no enlargement of lymph glands.

Thorax. The heart showed some excess of fat in the epicardium; the left ventricle showed some hypertrophy; there was no valvular disease. The lungs showed no abnormal appearances.

Abdomen. The spleen occupied the whole of the left hypochondrium; it weighed 66 ozs; it was dark purple in colour, hard and tense. On section, it looked like damson cheese. It gave no amyloid reaction. Under the microscope, a large quantity of granular brown pigment was diffused through the pulp, but there was no other structural change. The liver appeared healthy.

The /

The stomach was dilated, and its mucous membrane was covered with bile and mucus; it also contained some bile. The kidneys were rather large, their cortices looked dark, and the medullary portions pale. Under the microscope, pigment could be seen lying in the tubules. The suprarenal capsules were very small, and appeared very much atrophied. The semilunar ganglia were healthy, no change being detected microscopically. Vide table, p.

Table Applying to the Two Last Cases.

+ * W.E. (m)		
<hr/>		
+ * W.H.E. (m)	A.E (f)	+ * B.E (f)

All these patients lived in England, and had never been exposed to malaria.

- M = male.
 F = female.
 + = dark coloured urine.
 * = enlarged spleen.

CASE XVII.

(Recorded by Brühl 13.)

Increasing weakness; great enlargement of the spleen;
no changes in the lymph glands.

Reduction in the number of red blood corpuscles, and
amount of haemoglobin; no increase in the number of
white cells.

Inter-current attacks of pyrexia, vomiting and diar-
rhoea.

I.P., male, age 54, hatter. (Case taken July
 1890.)

Family History.

Parents both died at an advanced age; the family
 history is otherwise negative.

Previous History.

The patient is married and has several children
 who are all in good health. He has always enjoyed
 good health, and has never had malaria, nor been ex-
 posed to infection; he has always lived in Paris
 where he was born; he denies syphilis, nor does he
 show any trace of it.

Present Illness.

For about a year he has been losing his strength
 and appetite, suffering at times from intermittent
 attacks /

attacks of diarrhoea together with several paroxysms of abdominal pain. There have been frequent attacks of epistaxis, more or less severe. He remained at work till recently, when he had a more severe attack of pain in the left hypochondrium, with vomiting and nausea. The skin is a pale grey white; there has been no jaundice; there is some emaciation. The patient suffers from profuse perspirations and great weakness; walking is difficult and the least effort exhausts him.

State on Admission.

The patient appears very anaemic. Examination(a) of the abdomen shows considerable swelling in the left hypochondrium, which is found to be caused by a greatly enlarged spleen, which, in the epigastric region extends past the median line and reaches down to the level of the ant. sup. iliac spine, measuring in its largest diameter 28cm. Palpation shows that the splenic tumour is firm, the surface presenting, here and there, areas which are somewhat raised and harder. There is no particular tenderness on manipulation. There are two well-marked notches on the right border. The liver is also somewhat enlarged and projects below the costal margin, but is not tender on palpation. There /

There is no prominence of the superficial veins nor ascites. The tongue is clean, and the appetite except during the attacks, is good. There are no digestive troubles and the bowels are regular; (b) There is no enlargement of any of the lymphatic glands; (c) The heart does not present any abnormal feature. The pulse = 80, small but regular; (d) There seems to be impaired resonance towards the base of the left lung, with slightly diminished breath sounds and some friction; otherwise the respiratory system is healthy; (e) The urine varies in character, being at times light-coloured and clear, at others very dark; the quantity varies between 750 and 1,500 cc; the urea 1 per cent to 1.5 per cent; no sugar nor albumen found, but with nitric acid a distinct pink colour is given; (f) The nervous system is negative.

The blood:	R.B.C.	=	2,851,350
	W.B.C.	=	10,757
	Haematoblasts	=	93,000 (?)
	Haemoglobin	=	50 per cent.

The red discs show considerable variation in size with reduction in the amount of haemoglobin, but there is no appearance of poikilocytosis; no nucleated cells are /

are seen, the white corpuscles do not show any abnormal characters.

Progress of the Case.

During his stay in hospital, the patient had three attacks accompanied by pain, elevation of temperature, nausea, vomiting and profuse diarrhoea. The spleen became very tender and there was evidence of a subacute attack of pleuritis. For a period of five months the spleen increased in size; the patient became gradually weaker; oedema of the legs supervened, ending fatally. The duration was eighteen months since the first onset of weakness.

CASE XVIII.

(Recorded by Banti) (12).

Increasing Weakness.Great Enlargement of Spleen.No change in Lymph Glands.Anaemia.Death from Pneumonia.Autopsy.

Elizabeth C., 72, housewife.

Family History.

Negative.

Previous History.

The patient has always been healthy, never having any serious illness. She has never suffered from malaria nor has lived in ague districts. She has had no children; there is no history of syphilis. Her surroundings have always been healthy.

Present Illness.

This came on with a feeling of weakness which gradually became worse. After about a year she perceived a swelling in her left side; there was no diarrhoea at this time. She became so bad that she was obliged to go into hospital.

On examination, she is found to be very weak,
her /

her skin being of a yellow tinge, the conjunctivae white. No enlarged lymph glands can be felt anywhere.

Examination of the abdomen shows considerable enlargement of the spleen, which is oval in form, of firm consistence and smooth on the surface. Palpation is painless. The liver is also somewhat enlarged.

Examination of the lungs shows that the breath sounds are feeble all over the left base posteriorly.

Blowing murmurs are heard at the base of the heart.

Blood: R.B.C. = 3,720,000.

W.B.C. = 19,805.

Many red corpuscles are about 3μ - 4μ in size. No nucleated forms are seen.

The patient gradually became worse and finally developed acute pneumonia, and died.

Autopsy.

Lobar pneumonia of the left lung. The heart did not show any valvular disease, but the myocardium was in a condition of advanced fatty degeneration and very friable.

Peritoneum healthy; considerable catarrh of the gastro-intestinal surface, with thinning of the stomach /

stomach walls. The liver was enlarged, (2080 grms) red-brown. The spleen was greatly enlarged, but of the usual shape, firm. Weight 1255 grms. (normal = 200); on section, firm and of a deep red colour, showing small white points. No enlarged lymph glands were found. The other organs appeared healthy. The bone marrow in each femur was of a red colour, being foetal in appearance.

Microscopic Examination.

The liver showed increase of connective tissue in the portal spaces; the capillaries were dilated; the hepatic cells showed fatty granules; no lymphoid tissue was found.

The spleen showed increase of the trabeculae and the Malpighian corpuscles showed considerable sclerosis, the central arteriole being much thickened, and the splenic tissue adjacent to them being much more fibrous than normal. There was general thickening of the splenic reticulum, with reduction in the number of lymphoid cells.

The lymph glands did not show any change.

Bone marrow - Red and white corpuscles were seen in abundance, but no nucleated red cells. A few large cells were seen, showing a nucleus in division.

CASE XIX.

Banti (12).

Epistaxis.Increasing Asthenia.Enlargement of Spleen.Anaemia.Death.

David G., 18.

Previous History.

No hereditary illnesses; he has always enjoyed good health, and has never had malaria.

Present Illness.

This began a year previously, with a feeling of weakness and debility, with palpitation, but without any derangement of digestion.

Epistaxis was at times profuse.

On examination, the general tint is a yellow-waxen white.

The abdomen is enlarged, and on palpation a considerable tumour is felt in the left hypochondrium, which, by the usual methods, is found to be the spleen. Palpation is painless.

Blood: R.B.C. = 3,990,000.

W.B.C. = 4,704.

The /

The red cells are very pale and several appear of small size, but none are nucleated. The white are normal, and none contained any pigment.

The patient left the hospital and died at home. No autopsy could be obtained.

CASE XX.

Banti (12).

Increasing Asthenia.Epistaxis.Severe Diarrhoea.Anaemia.Enlargement of Spleen.Splenectomy.Death.Autopsy.

S.M., age 16, female.

Family History.

Parents enjoy good health; no hereditary illness.

Previous History.

The patient has enjoyed fair health and never has had, nor been exposed to malaria. There is no history of syphilis.

Present Illness.

For about two years, she has had a swelling in the left side and has been getting paler and weaker, and has suffered frequently from epistaxis and dysenteric diarrhoea.

Examination.

She is well developed, but very pale. There is considerable /

considerable increase in size of the spleen which reaches down as far as the iliac crest. In the peritoneal cavity there is much fluid effusion. No lymph glands are enlarged.

Blood: R.B.C. = 3,948,000.

W.B.C. = 6,876.

Splenectomy was performed, but the patient died from haemorrhage.

Autopsy.

Lungs healthy; heart shows yellow coloration of the myocardium; valves healthy.

Spleen = 1310 grms, greatly enlarged, but of usual shape, very firm and of a dark red colour. On section, the splenic tissue is dense, and shows small white points corresponding to the Malpighian corpuscles, the capsule and trabeculae being much thickened.

The liver does not appear enlarged. The other organs seem healthy; no abnormal lymph glands are found.

Microscopic Examination.

In the spleen there is much thickening of the fibrous framework with fibrosis of the Malpighian corpuscles, and sclerosis of the central arteriole. In the meshes of the reticulum are fewer corpuscles than usual. The liver showed some multilobular cirrhosis.

CASE XXI. (Recorded by Landouzy) (47).

Asthenia. Recurrent Epistaxis.

Enlargement of Spleen and Liver.

Reduction in number of R.B.C.

No increase of W.B.C.

Death.

Autopsy: Enlarged and indurated Spleen; Enlarged Liver.

A man, age 46, coachman, complained of great weakness and breathlessness.

Previous History.

There was no history of either alcoholic excess or venereal disease; the patient had never had any particular illness. For more than a year he had suffered from recurrent epistaxis.

On examination, there was a marked anaemic appearance, the skin having a somewhat yellow wax-like tint, and the mucous membranes being blanched. There was some headache with tinnitus aurium. The spleen showed great enlargement measuring about 20 cm. in length; the liver projected somewhat beyond the costal margin. The heart showed the conditions usual in anaemia. The urine was negative.

The /

The blood (examined by Malassez).

R.B.C. = 1,000,000.

W.B.C. = 3,200.

Progress of the Case.

The anaemia progressed and the patient died of syncope.

Autopsy.

There was great enlargement of the spleen, the organ being very firm. The liver was also considerably enlarged and showed traces of old perihepatitis.

The other organs did not show any special abnormality.

CASE XXII.

(Recorded by Woillez).(2)

Weakness. Intermittent Diarrhoea.Vomiting, Nausea and yellow colour of Skin.Enlargement of Spleen.Autopsy.

Bulletin de la Société Médicale des Hôpitaux, 1856.

Pierre G., age 40, mason.

Family and Previous History.

With the exception of some alcoholic excess in early life, the history is negative.

Present Illness.

About three months previous to his admission into hospital, the patient began to suffer from loss of strength, intermittent diarrhoea, irregular febrile attacks with slight rigors and sweats. A more severe attack than usual accompanied by vomiting, nausea and icteric coloration, brought him to hospital.

On examination, the patient was very anaemic-looking, olive-tinted (which soon passed off). There was slight oedema of the legs, and physical examination of the abdomen showed great enlargement of the spleen, which reached almost to the median line and extended /

extended downwards for about three inches below the level of the umbilicus. The organ was painful on palpation; its surface appeared smooth. The liver was not found to be increased in size; there was no prominence of the surface veins, nor was there any ascites. No enlarged lymph glands could be found anywhere. The heart showed some dilatation with haemic murmurs, etc.

The thyroid was not enlarged.

Examination of the blood did not show any increase in the white cells. (Number of red cells not stated).

Progress.

The cachectic condition increased rapidly with most severe prostration, ending in a comatose condition and death.

Autopsy.

There was a great enlargement of the spleen which measured 26 cm. in length, 12 cm. in breadth, and 5 cm in thickness, the organ being dark red, smooth and firm; on section it was fleshy, red and firm. The liver did not appear abnormal. The other organs seemed healthy. Two lymph glands in the mesocolon were somewhat enlarged but all the others appeared normal.

CASE XXIII.

(Recorded by Potain).(46)

A man, age 50, suffered from gradually increasing weakness.

Previous History.

He had never had any particular illness, but since his youth, had been liable to epistaxis.

Present Illness.

Four years ago he noticed that he was losing flesh and becoming very weak. In November 1885 he had albuminuria and in 1886 an attack of left sided pleuritis.

Examination.

anaemic

There is a marked appearance, feebleness, loss of flesh and dyspnoea. Haemic murmurs are heard over the base of the heart and in the veins of the neck. The spleen is much enlarged, measuring 23 cm. in length. The liver does not appear increased in size. There are no enlarged lymph glands anywhere.

Blood :- R.B.C. = 2,000,000

Haemoglobin = 30 per cent.

No increase of white corpuscles.

CASE XXIV. (Recorded by Strumpell) (23).

Asthenia; Vomiting and Diarrhoea with relapsing Anaemia.

Enlargement of Spleen; no glandular Enlargement.

Reduction in number of R.B.C., and amount of Haemoglobin.

Death.

Autopsy - Enlarged and indurated Spleen; Pigment in Liver Cells.

A man, age 25, servant, complained of vomiting, diarrhoea and weakness for about six months.

Previous History.

The patient was supposed to have had typhus four years previously. There was no history of alcoholism, syphilis nor malaria.

Present Illness.

Six months previously, he noticed that he was getting extremely weak, and losing his appetite. Vomiting, etc., supervened. On admission he appeared extremely anaemic. The spleen was found to be much enlarged, and examination of the blood showed absence of leucocytosis, but decrease in the number of red discs; the haemoglobin was reduced to 20 per cent /

cent. The anaemia steadily progressed and the spleen increased in size. The other signs and symptoms of anaemia were present.

Transfusion brought about considerable improvement with decrease in the size of the spleen.

In March 1876, after a period of quiescence of about three months, the patient had a relapse, the anaemia lasting for nearly two months.

Six months later, there was a third relapse. On each of these occasions there was increase in the size of the spleen. In December of that year (1876) the number of red discs was found to be 1,200,000.

The patient died the following April.

Autopsy.

There was general anaemia of all the organs. There was no ascites. The spleen, though smaller than during life was still much enlarged, and of a dark red colour and very firm. The capsule was smooth and did not show any areas of fibrous thickening. The liver was somewhat enlarged and anaemic. The bone marrow was deep red, somewhat dense. The lungs showed hypostatic pneumonia.

Microscopical examination of the spleen showed merely distension of some of the vessels.

CASE XXV.

(Recorded by Lodi).

The patient, a male, age 27, suffered from malarial attacks of a tertian type, during three months when he was thirteen. These did not recur after that period. At 23, he first began to suffer from a progressive anaemia with quiescent intervals.

On admission to hospital, he presented an extremely anaemic appearance, with the various cardiac conditions and dyspnoea. Examination of the abdomen showed great enlargement of the spleen, which measured 19 cm in length and 22 cm in breadth. There was also enlargement of the liver. The urine contained about 1.3% urea. There was an irregular evening temperature. Blood: R.B.C. = 1,820,000. This figure fell to 1,000,000, but there was no increase in the number of white cells.

Autopsy.

The spleen was much enlarged, and of a red-brown colour, firm on the surface, softer at the centre; the liver was enlarged, anaemic and fatty; the kidneys also were pale and fatty; the blood was acid.

Microscopical examination of the spleen, showed a great decrease of the Malpighian bodies with increase of the trabeculae and fibrous tissue of the organ. In the liver great fatty degeneration of the cells was found.

CASE XXVI.

(Recorded by Dégle).(49)

Extreme weakness; Vertigo; Epistaxis coming on after

Birth of Child; Vomiting and Diarrhoea.

Enlargement of Spleen and Liver.

No Enlarged Lymph Glands.

A woman, age 40., who had in early life been treated for chlorosis, had had ten children, all of whom she nursed.

The last confinement took place recently. For ten months she had been complaining of extreme weakness, vertigo, loss of appetite and frequent epistaxis, the paleness of the blood having attracted her attention. There was also vomiting with diarrhoea.

Examination.

The spleen was greatly increased in size, measuring 26 cm. in length; the liver was also enlarged projecting considerably beyond the costal margin. Both organs were tender on palpation.

No enlarged lymph glands could be found. The heart presented loud haemic murmurs, the blood resembled pale red serum, the red discs being greatly diminished (number not stated) but there was no increase /

increase of the white. The individual red cells showed decrease of haemoglobin. The anaemia and cachexia progressed rapidly. Oedema and dyspnoea became marked, albuminuria supervened. The case ended fatally. No autopsy.

CASE XXVII.

(Recorded by Müller.)(3)

Berl. Klin. Wochenschrift, 1867.

A man age 56, whose previous health had been good, began to complain a year before examination. of increasing weakness, loss of flesh and fatigue. These all seemed to come on without any appreciable cause.

On examination:

The spleen was much increased in size, and the liver dulness extended beyond the costal margin. On several occasions he suffered from attacks of local peritonitis in the splenic region. At a later date a generalised peritonitis came on which ended fatally.

Autopsy.

General peritonitis, which was found to be due to a perforating ulcer of the lower part of the jejunum. Great enlargement of the spleen, which was very firm, the capsule being much thickened. On section there were haemorrhagic infarcts but otherwise the structure appeared normal.

CASE XXVIII.

(Recorded by Müller.) (3)

Berl. Klin. Wochenschrift, 1867.

A man, age 56, complained for six years of recurrent pain in the left hypochondrium. There was at times a distinct subicteric tinge. A somewhat severe febrile attack with rigors, vomiting and severe abdominal pain brought him under observation.

On examination:

There was marked pallor of the skin and mucous membranes, loss of flesh, and great weakness. Examination of the abdomen showed great increase in the size of the spleen, this reaching to the umbilicus. The liver extended about two inches beyond the costal margin. There was no glandular enlargement. Examination of the blood did not show any increase in the number of white corpuscles. The urine contained traces of albumen.

Autopsy.

The spleen was greatly enlarged, filling the whole of the left side of the abdomen; the surface was smooth generally, but here and there were areas of local perisplenitis. The capsule as a whole was much thickened and the organ was very firm.

On /

On section, the spleen was of a red-brown colour and presented a uniform appearance, i.e., neither the connective tissue nor the Malpighian corpuscles being distinct; there were also several infarcts. The liver was enlarged, and its capsule thickened, but the surface was smooth, and on section, the organ was pale red. There was no enlargement of any of the internal lymph-glands. The other organs all appeared healthy.

Microscopical examination of the spleen shows that the enlargement is due to an increase in the connective tissue, with great thickening of the trabeculae and stroma. The number of lymphoid cells appeared to be decreased, and here and there were large cells undergoing fatty degeneration.

TABLE of CASES.

No	Name	Sex	Age of Onset	Dura- tion	By Whom Recorded	
1	E.N.———	f	21?	18yrs.	Douglas Stanley	
2	Jas. L.———	m	7?	14 "	" "	
3	Annie S.———	f	32?	1+"	" "	
4	Charlotte B.———	f	23	11+"	" "	
5	Alice H.———	f	9?	4+"	" "	
6	M.S.———	f	24	1+"	" "	
7	A.P.———	m	4	40+"	Wilson & Stanley	(16)
8	Alice P.———	f	5	5+"	" "	"
9	N.T.———	m	7	6+"	" "	"
10	R.T.———	m	7	6+"	" "	"
11	Mrs A.P.———	f	26(?)	37?"	C.Wilson	(11 vol) ?
12	Mrs T.———	f	7	39 "	Wilson & Stanley	(16)
13	Robert P.———	m	7?	2+"	Williamson	(17)
14	Jas.F.———	m	19?	2 "	"	"

TABLE of CASES. (Continued)

No	Name	Sex	Age of Onset	Dura- tion	By Whom Recorded	
15	W.H.E. —————	m	?	?yrs.	Saundby	(19)
16	B.E. —————	f	15?	3? "	"	"
17	Isidore P. ———	m	53?	1½ "	Bruhl	(13)
18	Eliz. C. —————	f	71?	1? "	Banti	(12)
19	D.G. —————	m	17?	1? "	"	"
20	S.M. —————	f	14?	2? "	"	"
21	—————	m	45?	? "	Landouzy	(47)
22	P.G. —————	m	40?	? "	Wuillez	(2)
23	—————	m	46?	4? "	Potain	(46)
24	—————	m	24½	2½? "	Strümpell	(23)
25	—————	m	23?	4? "	Lodi	(48)
26	—————	f	39?	1? "	Degle	(49)
27	—————	m	50	6? "	Muller	(3)
28	—————	m	55?	1 "	"	"

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